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OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

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Subject: Myclobutanil. Human-Health Risk Assessment for Proposed Use on Section 3 Requests for Use on Snap Bean, Mint, Papaya, Gooseberry, Currant, Caneberry, Bell and Non-Bell Pepper, Head and Leaf Lettuce, and Artichoke.

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Risk Assessment Type: Single Chemical Aggregate

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From: W. Cutchin, Acting Branch Senior Scientist
M. Dow, Ph. D., Biologist
Alternative Risk Integration Assessment Team (ARIA)
Risk Integration, Minor Use & Emergency Response Branch (RIMUERB)
Registration Division (RD; 7505P)

Thru: D. Vogel, Branch Chief
Registration Action Branch 1 (RAB1)
Health Effects Division (HED; 7509P)

To: Barbara Madden, RM Team 05
RIMUERB/RD (7505P)

INTRODUCTION

The ARIA Team of the Office of Pesticide Programs (OPP) is charged with estimating the risk to human health from exposure to pesticides. The RD of OPP has requested that ARIA evaluate hazard and exposure data and conduct dietary, occupational, residential and aggregate exposure assessments, as needed, to estimate the risk to human health that will result from proposed and registered uses of the pesticide myclobutanil [α-butyl-α-(4-chlorophenyl)-1*H*-1,2,4-triazole-1-propanenitrile] as a result of the proposed uses on crop group 8, except tomato; okra; crop subgroup 4A, except spinach; cilantro; artichoke; papaya; black sapote; canistel; mamey sapote; mango; sapodilla; and star apple. In addition, data has been submitted in support of the requests to remove the conditions of registration for myclobutanil on bean, snap, succulent; peppermint and spearmint; gooseberry; current; and caneberry. A summary of the findings and an

assessment of human risk resulting from the registered and proposed tolerances for myclobutanil is provided in this document. The risk assessment, residue chemistry data review, and the dietary risk assessment is by W. Cutchin (ARIA), the occupational/residential exposure assessment by M. Dow (ARIA), and the drinking water assessment by J.Wolf (Environmental Fate and Effects Division; EFED).

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1.0 Executive Summary

The Interregional Research Project No. 4 (IR-4) has submitted petitions for the use of myclobutanil [α-butyl-α-(4-chlorophenyl)-1*H*-1,2,4-triazole-1-propanenitrile] and the establishment of permanent tolerances for the combined residues of myclobutanil and its alcohol metabolite, RH-9090 [α-(3-hydroxybutyl)-α-(4-chlorophenyl)-1*H*-1,2,4-triazole-1-propanenitrile] 6-chloro-3-pyridinyl)methyl]-*N*-nitro-2-imidazolidinimine, expressed as the parent, in/on papaya, bell and non-bell pepper, head and leaf lettuce, and artichoke. In addition, IR-4 has submitted data in support of the requests to remove the conditions of registration for myclobutanil on bean, snap, succulent; peppermint and spearmint; gooseberry; current; and caneberry. Aggregate risk assessments were performed for acute (food and drinking water), short-term (food, drinking water and residential), intermediate-term (food, drinking water and residential), and chronic aggregate exposure (food and drinking water). The aggregate risks associated with the proposed uses of myclobutanil are not of concern to HED for the general U.S. population or any population subgroup.

Use Profile

Myclobutanil is a contact fungicide that is applied to prevent fungal outbreaks. In agricultural and commercial settings, it has a variety of uses including fruits, vegetables, ornamentals, and turf. In the residential setting, the existing uses include turf and ornamentals. Permanent tolerances are currently established for the combined residues of myclobutanil and its RH-9090 metabolite (free and bound) in/on a variety of raw agricultural commodities (RACs) at levels ranging from 0.02 to 25.0 ppm and in meat, milk, poultry, and eggs at levels ranging from 0.02 to 1.0 ppm [40 CFR §180.443(a)]. In addition, tolerances in conjunction with Section 18 registrations have been established for a number of RACs under 40 CFR §180.443(b). Tolerances for indirect or inadvertent residues of myclobutanil have been established for several crop groups under 40 CFR §180.443(d). The proposed uses range from caneberries treated with four applications at 0.03 to 0.60 lb ai/A (0.25 lb ai/A, total rate) with 10-14 days retreatment interval (RTI) and a 0-day preharvest interval (PHI) to papayas treated with eight applications at 0.25 lb ai/A (2.0 lb ai/A, total rate) with 13-15 days RTI and a 0-day PHI.

Toxicity/Hazard

The toxicological database for myclobutanil is adequate to support registration and tolerances. There are no data gaps. Myclobutanil has low acute toxicity with the exception for ocular irritation. It is Toxicity Category III for oral acute toxicity, and Category IV for dermal and inhalation acute toxicity and dermal irritation. Myclobutanil is Category I for ocular irritation and the technical is a dermal sensitizer. In rat subchronic and chronic toxicity studies, the primary target organs are liver and testes. Liver effects, following subchronic exposure, include hypertrophy, hepatocellular necrosis and increased liver weight. Chronic exposure to the rat also results in hepatocellular vacuolization and additional testicular effects, which include bilateral aspermatogenesis, increased incidences of hypospermia and cellular debris in the epididymides and increased incidences of arteritis/periarteritis in the testes. With the exception of testicular effects, subchronic and chronic exposures in the mouse result in a toxicity profile similar to the

rat. The mouse, following chronic exposure, has, in addition, increased Kupffer cell pigmentation, periportal punctate vacuolation, and individual cell necrosis of the liver. There is no evidence of carcinogenic potential in either the rat or mouse. In the subchronic dog, there are hepatocellular hypertrophy, increased relative and absolute liver weight and increased alkaline phosphatase. In the chronic dog study, liver toxicity is similar with the addition of "ballooned" hepatocytes and increases in serum glutamic pyruvic transaminase (SGPT) and gamma glutamyl transferase (GGT). Signs of toxicity observed in the rat 28-day dermal studies are limited to dermal irritation. There is no evidence of systemic toxicity in either study. There is no evidence of increased susceptibility in either of the developmental toxicity studies or the reproduction study. In the rat developmental toxicity study, maternal toxicity, which included rough hair coat and salivation, occurs at the same dose level as increases in incidences of 14th rudimentary and 7th cervical ribs in the fetuses. At the next higher dose there is also alopecia, desquamation and red exudate around the mouth in the dams. In the rabbit developmental toxicity study there is reduced body weight and body weight gain during the dosing period, clinical signs of toxicity and a possible increase in abortions in the does at the same dose level that there are increased resorptions, decreased litter size and decreased viability index. The maternal toxicity in the rat reproduction study includes increased liver weights and hepatocellular hypertrophy. Reproductive effects occur at the same dose and include increased incidences in the number of still born pups and atrophy of the testes, epididymides and prostate. Developmental effects occurring at the same dose in the reproduction study include decreased pup body weight gain during lactation. Myclobutanil is rapidly absorbed and excreted with complete elimination by 96 hours. There is extensive metabolism prior to excretion with elimination of radiolabeled material evenly distributed between urine and feces. There is no evidence of tissue accumulation. There is no concern for mutagenic activity. Myclobutanil was determined to be not carcinogenic in two acceptable animal studies. Therefore, it was classified as a "Group E" chemical (evidence of noncarcinogenicity for humans).

RAB1 toxicologists recently re-evaluated the myclobutanil toxicology database and concluded that the 28-day dermal toxicity study previously used for short-term dermal risk assessment is not appropriate. A two-generation reproduction study in rats was selected because the effects of concern (atrophy of the testes and prostate) seen at a lowest observed adverse effect level (LOAEL) of 50 mg/kg/day may not be protective if the endpoints were based on the 28-day dermal toxicity study. In addition, there were no effects of concern identified in the 28-day dermal toxicity study [no observed adverse effect level (NOAEL) of 100 mg/kg/day was the highest dose tested]. HED evaluated the hazard and exposure data for myclobutanil and recommended that the FQPA Safety Factor (SF) be reduced to 1x in assessing the risk posed by this chemical. The doses and toxicological endpoints selected for various exposure scenarios are summarized below.

Exposure Scenario	Dose Used in Risk Assessment, UF	FQPA SF and Endpoint for Risk Assessment	Study and Toxicological Effects

Acute Dietary females 13-50 years of age	NOAEL = 60 mg/kg/day UF = 100 Acute RfD = 0.60 mg/kg/day	FQPA SF = 1x aPAD = acute RfD / FQPA SF = 0.60 mg/kg/day	Increased resorptions, decreased litter size and a decrease in the viability index.
Acute Dietary general population including infants and children	None	not applicable	not applicable
Chronic Dietary all populations	NOAEL= 2.49 mg/kg/day UF = 100 Chronic RfD = 0.025 mg/kg/day	FQPA SF = 1x cPAD = chronic RfD / FQPA SF = 0.025 mg/kg/day	Decreased testicular weights and increased testicular atrophy.
Short-Term Dermal & Inhalation (1-30 days) (Occupational/ Residential)	oral study NOAEL= 10 mg/kg/day (dermal absorption rate = 50%) (inhalation absorption rate = 100%)	acceptable MOE = 100 (Occupational) acceptable MOE = 100 (Residential, includes the FQPA SF)	Atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a decrease in pup weight gain during lactation.
Intermediate-Term Dermal & Inhalation (1-6 months) (Occupational/ Residential)	oral study NOAEL= 10 mg/kg/day (dermal absorption rate = 50%) (inhalation absorption rate = 100%)	acceptable MOE = 100 (Occupational) acceptable MOE = 100 (Residential, includes the FQPA SF)	Atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a decrease in pup weight gain during lactation.
Long-Term Dermal & Inhalation (> 6 months) (Occupational/ Residential)	oral study NOAEL= 2.49 mg/kg/day (dermal absorption rate = 50%) (inhalation absorption rate = 100%)	acceptable MOE = 100 (Occupational) acceptable MOE = 100 (Residential, includes the FQPA SF)	Decreased testicular weights and increased testicular atrophy.
Cancer (oral, dermal, inhalation)	"Group E"	not applicable	not applicable

Dietary Exposure (Food/Water)

Food

The nature of the residue in the subject crops, water, rotational crops, and livestock is adequately understood. The residues of concern in plants are the parent myclobutanil and its RH-9090 metabolite (free and bound). The residues of concern in livestock commodities except milk are myclobutanil and its metabolite α-(3-hydroxybutyl)-α-(4-chlorophenyl)-1*H*-1,2,4-triazole-1-propanenitrile (free). The residues of concern in milk are myclobutanil [α-butyl-α-(4-chlorophenyl)-1*H* -1,2,4-triazole-1-propanenitrile] and its metabolites, α-(3-hydroxybutyl)-α-(4-chlorophenyl)-1*H*-1,2,4-triazole-1-propanenitrile (free and bound) and α-(4-chlorophenyl)-α-

(3,4-dihydroxybutyl)-1*H* -1,2,4-triazole-1-propanenitrile. The residues of concern in rotational crops are the parent myclobutanil and its RH-9090 metabolite (free and bound).

An adequate enforcement method (Method 34S-88-10) is available to enforce the proposed tolerances. Quantitation is by gas chromatography using a nitrogen/phosphorus detector (GC/NPD) for myclobutanil and an electron capture detector (GC/ECD) for residues measured as the alcohol metabolite. Crop field trial samples were analyzed for residues of myclobutanil and its metabolite RH-9090 using a method derived from the enforcement method. The lower limit of method validation (LLMV) for both myclobutanil and its metabolite RH-9090 was 0.01 ppm in lettuce (head and leaf) and artichoke; 0.02 ppm in pepper (bell and non-bell), caneberry, gooseberry, and snap bean. The LLMV for currant was 0.0199 ppm for myclobutanil and 0.0204 ppm for RH9090. The LLMV for papaya was 0.0199 ppm for myclobutanil and 0.0204 ppm for RH9090. The LLMV for mint was 0.019 ppm for myclobutanil and 0.02 for RH9090. The method used for data collection, based on the enforcement method, 34S-88-10, is adequate. There are adequate storage stability data to support the requested uses. None of the raw agricultural commodities of the subject petitions have associated livestock feed items of regulatory concern. The petitioner has submitted adequate crop field trial and processing studies to support their requested uses of myclobutanil.

Snap Beans

The results from the snap bean trials show that the highest total myclobutanil residues were 0.40 ppm in samples treated at the seasonal rate of 0.50 lb ai/A and harvested the day of the final application. The new snap bean data are submitted to remove the conditional registration. ARIA recommends that the conditional registration for myclobutanil on bean, snap, succulent be removed.

Mint

The results from the mint trials show that the highest total myclobutanil residues were 0.24 ppm in samples treated at the seasonal rate of 0.382 lb ai/A and harvested at 31 days after the final application.

The mint data are submitted to remove the conditional registration. ARIA recommends that the conditional registration for myclobutanil on mint be removed.

Papaya

The results from the papaya trials show that the highest total myclobutanil residues were 1.95 ppm on a sample treated at the seasonal rate of 2.0 lb ai/A and harvested the day of the final application. There is adequate number and geographic location of residue field trials to support a tolerance registration on papaya and the data also support tolerance for black sapote, canistel, mamey sapote, mango, sapodilla, and star apple as requested by the petitioner. However, the requested tolerances are not appropriate. **A revised Section F is required for the residues of myclobutanil on papaya, sapote, canistel, mamey sapote, mango, sapodilla, and star apple at 3.0 ppm.**

Gooseberry

IR-4 has submitted field trial data for myclobutanil on gooseberry. At each trial location, gooseberries received eight foliar applications at a single application rate of 0.122 to 0.136 lb ai/A (seasonal rate of 1.04 to 1.05 lb ai/A) with 10 to 14 days between applications and a 0-day PHI. The results from these trials show that the highest total myclobutanil residues were 0.35 ppm in samples treated at the seasonal rate of ~1.00 lb ai/A and harvested the day of the final application.

The gooseberry data are submitted to remove the conditional registration. The data are adequate in number and geographic location to satisfy the requirements as requested in the cited memo. ARIA recommends that the conditional registration for myclobutanil on gooseberry be removed. Since the additional data does not exceed the established tolerances, no change in the existing gooseberry tolerance is required.

Current

IR-4 has submitted field trial data for myclobutanil on currant. At the trial location, currants received eight foliar applications at a single application rate of 0.125 to 0.130 lb ai/A (1.01 lb ai/A, total rate) with 13 and 15 days between applications and a 0-day PHI. The results from these trials show that the highest total myclobutanil residues were 1.05 ppm in samples treated at the seasonal rate of ~1.0 lb ai/A and harvested the day of the final application.

The current data are submitted to remove the conditional registration. The data are adequate in number and geographic location to satisfy the requirements as requested in the cited memo. ARIA recommends that the conditional registration for myclobutanil on current be removed. Since the additional data does not exceed the established tolerances, no change in the existing current tolerance is required.

Caneberry

IR-4 has submitted field trial data for myclobutanil on caneberry. At each trial location, caneberries received four foliar applications at a single application rate of 0.060 to 0.068 lb ai/A (seasonal rate of 0.244 to 0.257 lb ai/A) with 10 to 14 days between applications and a PHI of 0 days. The results from these trials show that the highest total myclobutanil residues were 0.62 ppm in samples treated at the seasonal rate of ~0.25 lb ai/A and harvested the day of the final application.

The caneberry data are submitted to remove the conditional registration. The data are adequate in number and geographic location to satisfy the requirements as requested in the cited memo. ARIA recommends that the conditional registration for myclobutanil on caneberry be removed. Since the additional data does not exceed the established tolerance, no change in the existing caneberry tolerance is required.

Bell and Non-Bell Pepper

IR-4 has submitted field trial data for myclobutanil on bell and non-bell pepper. Bell peppers were grown in five trials and non-bell peppers were grown in one trial. At each trial, peppers were treated with four foliar applications at the approximate rate of 0.125 lb ai/A for a total of approximately 0.50 lb ai/A. The applications were made at 12 to16-day intervals and a 0-day

PHI. The analytical results show that the highest total myclobutanil residues were 0.19 ppm on bell pepper and 0.14 ppm on non-bell pepper sampled at the 0-day PHI. Also, RH-9090 residues were less than the LLMV of 0.02 ppm in all samples.

A total of 6 field trials on bell and non-bell peppers were previously conducted. Pepper plots received 4 foliar applications of myclobutanil at rates of ~0.125 lb. ai/A (0.5 lb ai/A/season). The applications were made at intervals of 13-15 days and mature peppers were collected following the final application or 1 day later. In bell peppers, myclobutanil and RH-9090 residues ranges were 0.02- 0.51 ppm and <0.02-0.17 ppm, respectively. In the non-bell peppers, myclobutanil and RH-9090 residues ranges were 0.08-2.03 ppm and 0.03-0.39 ppm, respectively. The previous data are used to support a tolerance with regional registration for myclobutanil on bell and non-bell peppers.

Using both the previously submitted data and the data in the current submission, there is adequate number and geographic location of residue field trials to support a tolerance with a national registration on peppers. In addition, the data also support a tolerance for fruiting vegetables (except cucurbits), crop group 8, except tomato since bell and non-bell peppers are the representative crop. However, the requested tolerances are not appropriate. In addition, the commodity definition is incorrect. **A revised Section F is required for the residues of myclobutanil on fruiting vegetables (except cucurbits), crop group 8, except tomato at 4.0 ppm.**

Okra

No data have been submitted for the residues of myclobutanil on okra. Okra is not currently a member of the fruiting vegetables crop group; however, IR-4 has submitted a Crop Group amendment to EPA to add okra to the fruiting vegetables crop group. HED has previously determined that field residue data for non-bell peppers is applicable to okra (DP Num: 274312, G. Herndon, 4/30/01). The previous bell and non-bell pepper data are used to support an okra tolerance with regional registration for myclobutanil in the following states: Texas, Oklahoma, Arkansas, New Mexico, Colorado, Arizona, Utah, Nevada, and California.

ARIA concludes that the data for the fruiting vegetables (except cucurbits) are adequate to support the requested tolerance on okra. However, the proposed tolerance is not appropriate. **A revised Section F is required for the residues of myclobutanil on okra at 4.0 ppm.**

Head and Leaf Lettuce

IR-4 has submitted field trial data for myclobutanil on lettuce (head and leaf). Fourteen field trials including seven head lettuce trials and seven leaf lettuce trials were conducted. At each trial, lettuce was treated with four foliar applications of myclobutanil at the approximate rate of 0.125 lb ai/A for a total of approximately 0.50 lb ai/A. The foliar applications were made at 12 to15-day intervals. Commercially mature lettuce samples were collected 2-4 days after the final application. Leaf lettuce samples for decline determination were also collected at approximately 0, 7, and 14 days following the final application. In the head lettuce trials, wrapper leaves were removed from half of the samples. Maximum myclobutanil residues on head lettuce at 2-4 day PHI were 1.36 ppm with wrapper leaves and 0.25 ppm without wrapper leaves. Maximum

myclobutanil residues on leaf lettuce at 2-4 day PHI were 4.03 ppm. Myclobutanil and RH-9090 residues declined significantly from 0-14 day PHI on leaf lettuce.

There is an adequate number and geographic location of residue field trials on head and leaf lettuce, the representative crops to support a tolerance on leafy greens, crop subgroup 4A, except spinach. However, the requested tolerances are not appropriate. In addition, the commodity definition is incorrect. **A revised Section F is required for the residues of myclobutanil on leafy greens, crop subgroup 4A, except spinach at 9.0 ppm.**

Cilantro

No data have been submitted for the residues of myclobutanil on cilantro. Cilantro is not currently a member of the leafy greens, crop subgroup 4A, except spinach. However, since data for parsley has been determined to be adequate to support tolerances on cilantro (Reviewer's Guide, B. Schneider, 6/14/02) and parsley is a member of crop subgroup 4A, the data for head and leaf lettuce are adequate to support a tolerance on cilantro.

ARIA concludes that the data for the head and leaf lettuce (except cucurbits) are adequate to support the requested tolerance on cilantro. However, the proposed tolerance on cilantro is not appropriate. **A revised Section F is required for the residues of myclobutanil on cilantro at 9.0 ppm.**

Artichoke

IR-4 has submitted field trial data for myclobutanil on artichokes. Three field trials were conducted. At each trial, artichokes were treated with six foliar-directed applications of myclobutanil at the approximate rate of 0.1 lb ai/A for a total of approximately 0.6 lb ai/A. The foliar applications were made at 12- to 16-day intervals. Commercially mature artichoke samples were collected 3 days after the final application. The analytical results show that the highest total myclobutanil residues were 0.60 ppm in treated artichoke samples.

There is an adequate number and geographic location of residue field trials on artichoke. The requested tolerances are appropriate. ARIA recommends for the proposed myclobutanil tolerance of 0.90 ppm on artichokes.

There are no current Codex, Canadian or Mexican MRLs for residues of myclobutanil in/on any crops. Therefore, international harmonization is not an issue with these petitions.

Water

EFED provided Estimated Drinking Water Concentrations (EDWCs) of myclobutanil in surface and ground water using PRZM-EXAMS and Screening Concentration in Ground Water (SCI-GROW), respectively. The assessment was based on tropical fruit, which has the highest use rate among all existing uses. EFED calculated the 1- in 10-year peak acute and 1- in 10-year estimated annual mean non-cancer chronic EDWCs for myclobutanil in surface water to be 120.1 ppb and 46.3 ppb, respectively. The ground water EDWC for both acute and chronic exposures is estimated as 2.83 ppb.

Dietary Risk Analysis

An acute dietary exposure assessment was performed for females 13-49 years old (no endpoint was identified for the general U.S. population or any other population subgroup) using tolerance-level residues and 100% CT information for all registered and proposed uses. Drinking water was incorporated directly in the dietary assessment. These assessments conclude that the acute dietary exposure estimates (95th percentile) are below HED's level of concern (<100% of the acute population adjusted dose (aPAD)) for females 13-49 years old at 4% of the aPAD.

A refined, chronic dietary exposure assessment was performed for the general U.S. population and various population subgroups using some monitoring data, registered and proposed tolerances for other commodities; and some average percent crop treated (%CT) information. Drinking water was incorporated directly into the dietary assessment using the chronic concentration for surface water. This assessment concludes that the chronic dietary exposure estimates are below HED's level of concern (<100% of the chronic population adjusted dose (cPAD)) for the general U.S. population (20% of the cPAD) and all population subgroups. The most highly exposed population subgroup is children 1-2 years old at 30% of the cPAD.

Residential Exposure

All residential handler exposures and risks resulted in margins of exposure (MOEs) of >100; and, therefore, are not of concern to HED. The residential handler assessment was based upon the residential SOPs, the Pesticide Handlers Exposure Database (PHED), data, and Outdoor Residential Exposure Task Force (ORETF) study data. All residential post-application exposures and risks resulted in MOEs of >100; and, therefore, are not of concern to HED. The residential post-application assessment was based upon standard assumption from residential SOPs, the results of two dislodgeable foliar residue (DFR) studies on grapes in California, and turf transferable residue (TTR) data, when applicable.

Aggregate Risk

The acute aggregate risk assessment takes into account exposure estimates from dietary consumption of myclobutanil (food and drinking water). The acute dietary exposure estimates, which include drinking water, are below HED's level of concern (<100% aPAD) at the 95th exposure percentile for females 13-49 years old at 4% of the aPAD.

The short-term aggregate risk assessments estimate risks likely to result from 1-30 days of exposure to myclobutanil residues in food, drinking water, and residential pesticide uses. For adults, there is potential for short-term dermal and inhalation handler exposure, and short-term dermal post-application exposures from the residential uses of myclobutanil, including orchards, "pick your own" gardens, home fruit and vegetable gardens, and treated turf. For children/toddlers, short-term dermal and non-dietary oral post-application exposures may result from dermal contact with treated turf as well as non-dietary ingestion/hand-to-mouth transfer of residues from turf grass. For the general U.S. population and all population subgroup, including

infants and children, all short-term MOEs are greater than 100; and, therefore, are not of concern to HED (MOE <100).

The intermediate-term aggregate risk assessment estimates risks likely to result from 1-6 months exposure to myclobutanil residues in food, drinking water, and residential pesticide scenarios. For adults, intermediate-term post-application exposures may result from dermal contact with treated fruits and vegetables at "pick your own" gardens, treated home fruit and vegetable gardens and treated turf. Since myclobutanil is applied at 7- to 14-day intervals, only short-term exposure is expected for the residential handler. Therefore, no aggregate intermediate-term exposure for the adult handler was performed. For toddlers, intermediate-term dermal and non-dietary oral post-application exposures may result from dermal contact with treated turf as well as non-dietary ingestion/hand-to-mouth transfer of residues from turf grass. For the general U.S. population and all population subgroup, including infants and children, all intermediate-term MOEs are greater than 100; and, therefore, are not of concern to HED (MOE <100).

The chronic aggregate risk assessment takes into account average exposure estimates from dietary consumption of myclobutanil (food and drinking water) and residential uses. However, due to the use patterns, no chronic residential exposures are expected. Therefore, the chronic aggregate risk assessment includes exposure from food and drinking water only. The chronic dietary exposure estimates are below HED's level of concern (<100% cPAD) for the general U.S. population (20% of the cPAD) and all population subgroups. The most highly exposed population subgroup is children 1-2 years old at 30% of the cPAD. Therefore, the chronic aggregate risk associated with the proposed uses of myclobutanil are not of concern to HED for the general U.S. population or any population subgroups.

Occupational Exposure/Risk

Based upon the proposed new use patterns, ARIA believes the most likely methods of application are likely to be by ground boom and by airblast. The Rally® "parent" (i.e., not supplemental labels) label indicates that chemigation and aerial applications are permitted. ARIA expects the most highly exposed occupational handlers would most likely be mixer/loaders loading wettable powder packaged in water soluble packaging, applicators using open-cab ground-boom and open-cab airblast spray machinery and aerial applicators. It is possible for agricultural workers to have post-application exposures to pesticide residues during the course of typical agricultural activities. HED has identified a number of post-application agricultural activities that may occur and which may result in post-application exposures to pesticide residues. A MOE of 100 is adequate to protect occupational pesticide handlers and agricultural workers from post-application exposures. Since the estimated MOEs are > 100, the proposed uses are not of concern to ARIA.

Myclobutanil is classified in Acute Toxicity Category I for primary eye irritation and in Acute Toxicity Category IV for acute dermal toxicity, acute inhalation toxicity and primary skin irritation. It is a dermal sensitizer. The labels list a 24-hour reentry interval (REI). **The 24-hour REI listed on the product labels should be confirmed or corrected as may be necessary.**

Environmental Justice Considerations

Potential areas of environmental justice concerns, to the extent possible, were considered in this human health risk assessment, in accordance with U.S. Executive Order 12898, "Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations," http://www.eh.doe.gov/oepa/guidance/justice/eo12898.pdf).

As a part of every pesticide risk assessment, OPP considers a large variety of consumer subgroups according to well-established procedures. In line with OPP policy, ARIA estimates risks to population subgroups from pesticide exposures that are based on patterns of that subgroup's food and water consumption, and activities in and around the home that involve pesticide use in a residential setting. Extensive data on food consumption patterns are compiled by the USDA under the Continuing Survey of Food Intake by Individuals (CSFII) and are used in pesticide risk assessments for all registered food uses of a pesticide. These data are analyzed and categorized by subgroups based on age, season of the year, ethnic group, and region of the country. Additionally, OPP is able to assess dietary exposure to smaller, specialized subgroups and exposure assessments are performed when conditions or circumstances warrant. Whenever appropriate, non-dietary exposures based on home use of pesticide products and associated risks for adult applicators and for toddlers, youths, and adults entering or playing on treated areas postapplication are evaluated. Further considerations are currently in development as OPP has committed resources and expertise to the development of specialized software and models that consider exposure to bystanders and farm workers as well as lifestyle and traditional dietary patterns among specific subgroups.

Review of Human Research

This risk assessment relies in part on data from studies in which adult human subjects were intentionally exposed to a pesticide or other chemical. These studies (listed in Attachment B) have been determined to require a review of their ethical conduct, and have received that review.

Regulatory Recommendations and Data Deficiencies

Recommendations

Pending the results of the forthcoming triazole and metabolite risk assessment and provided the Section F is revised (see below), the residue chemistry, toxicological and occupational/residential databases are adequate to support the permanent tolerances for the combined residues of myclobutanil and its alcohol metabolite α- (3-hydroxybutyl)-α- (4-chlorophenyl)-1*H*-1, 2,4-triazole-1-propanenitrile (free and bound) in

Commodity	Tolerance (ppm)
Fruiting vegetables (except cucurbits), crop group 8, except tomato	4.0
Okra	4.0

Leafy greens, crop subgroup 4A, except spinach	9.0
Cilantro	9.0
Artichoke	0.90
Papaya	3.0
Black sapote	3.0
Canistel	3.0
Mamey sapote	3.0
Mango	3.0
Sapodilla	3.0
Star apple	3.0

In addition, the submitted data supports the removal of the conditions of registrations for myclobutanil on bean, snap, succulent; peppermint and spearmint; gooseberry; current; and caneberry. Since the additional data does not exceed the established tolerances, no change in the existing tolerances is required.

Deficiencies

A revised Section F is required for the residues of myclobutanil on papaya, sapote, canistel, mamey sapote, mango, sapodilla, and star apple at 3.0 ppm.

A revised Section F is required for the residues of myclobutanil on fruiting vegetables (except cucurbits), crop group 8, except tomato at 4.0 ppm.

A revised Section F is required for the residues of myclobutanil on okra at 4.0 ppm.

A revised Section F is required for the residues of myclobutanil on leafy greens, crop subgroup 4A, except spinach at 9.0 ppm.

A revised Section F is required for the residues of myclobutanil on cilantro at 9.0 ppm.

ARIA suggests that the RD confirm or correct, as may be necessary, the 24-hour restricted entry interval (REI) listed on the product label.

Completion of the triazole and metabolite risk assessment.

2.0 Ingredient Profile

2.1 Summary of Registered/Proposed Uses

Registered Uses: Myclobutanil is a contact fungicide that is applied to prevent fungal outbreaks. In agricultural and commercial settings, it has a variety of uses including fruits, vegetables, ornamentals, and turf. In the residential setting, the existing uses include turf and ornamentals. Permanent tolerances are currently established for the combined residues of myclobutanil and its

RH-9090 metabolite (free and bound) in/on a variety of RACs at levels ranging from 0.02 to 25.0 ppm and in meat, milk, poultry, and eggs at levels ranging from 0.02 to 1.0 ppm [40 CFR §180.443(a)]. In addition, tolerances in conjunction with Section 18 registrations have been established for a number of RACs under 40 CFR §180.443(b). Tolerances for indirect or inadvertent residues of myclobutanil have been established for several crop groups under 40 CFR §180.443(d).

Proposed Uses: A specimen label was provided for Nova™ 40 WSP, a product containing 40% ai. Table 2.1 is a summary of the proposed use pattern.

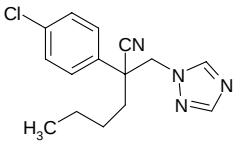
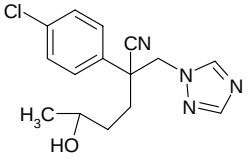
Table 2.1. Summary of Proposed Use Patterns.

Crop	Product (EPA Reg. No.)	**# App.**	**Application Rate (lb ai/A)**		**RTI[1] (days)**	**PHI[1] (days)**	**Restrictions**
			Per app.	**Per season**			
Snap Bean	Nova 40 W (62719-411)	4	0.125	0.5	7-10	0	Rust: Begin at first observation. Pod tip rot: Begin at pod development and continue at 7-10 day intervals
Mint	Nova 40 W (62719-411)	3	0.125	0.375	14-21	30	Begin applications in early spring when plants break dormancy.
Papaya	Nova 40 W (62719-411)	8	0.25	2.0	14	0	Do not plant any crop other than those on the label for 12 months following the last application.
Gooseberry	Nova 40 W (62719-411	8	0.125	1.0	10-14	0	Anthracnose: Begin at unfolded first leaf then at 10-14 intervals. Powdery mildew: Make applications at pre-bloom, full bloom and 2 weeks later.
Current	Nova 40 W (62719-411)	3	0.125	1.0	NA	0	Make applications at pre-bloom, full bloom and 2 weeks later.
Blackberry & Raspberry	Nova 40 W (62719-411)	4	0.03-0.06	0.25	10-14	0	Apply at budbreak. Use shorter interval under heavy disease pressure.
Fruiting vegetables, crop group 8, except tomato and okra	NOVA 40W (62719-411)	4	0.0625 to 0.125	1.25	10-14	0	Apply the lower rate when plants are small. Increase the rate as plants increase in size.
Crop subgroup 4A, except spinach	NOVA 40W (62719-411)	4	0.0625-0.125	1.25	10-14	3	Apply the lower rate when plants are small. Increase the rate as plants increase in size.
Artichoke	Nova 40 W (62719-411)	6	0.075 - 0.1	0.6	14	3	Apply the lower rate when plants are small. Increase the rate as plants increase in size.

[1] RTI = retreatment interval; PHI = preharvest interval; GPA = gallons per acre.

The label specifies the following rotational crop restrictions: Fields treated with myclobutanil can be rotated at any time to crops that are listed on a registered myclobutanil label immediately after the last treatment. Do not plant other crops within 30 days after the last application of a product containing myclobutanil. The proposed use directions are adequate and supported by the available residue chemistry data.

2.2 Structure and Nomenclature

Table 2.2.a Myclobutanil Nomenclature.	
Chemical structure	
Common name	Myclobutanil
Company experimental name	RH-3866
IUPAC name	(*RS*)-2-(4-chlorophenyl)-2-(1*H*-1,2,4-triazol-1-ylmethyl)hexanenitrile
CAS name	∝-butyl-∝(4-chlorophenyl)-1*H*-1,2,4-triazole-1-propanenitrile
CAS #	88671-89-0
End-use product/(EP)	Rally 40 W (EPA Reg. No. 62719-411), NOVA 40W (EPA Reg. No. 62719-411)
Chemical structure of regulated metabolite	
Common name	Alcohol metabolite
Company experimental name	RH-9090

2.3 Physical and Chemical Properties

Table 2.3 Physicochemical Properties of the Technical Myclobutanil.		
Parameter	**Value**	**Reference**
Melting range/range	63-68 °C	Product Chemistry Review (C.L. Trichilo, 1988), and Rohm and Haas Report, "Revision to: RH-3866 Technical - Physical and Chemical Characteristics"
pH	The technical material cannot be diluted or dispersed in water. The pH of a saturated aqueous solution of this material is about 6-7, the same as the background value of the water used.	
Density	1.22 g/cc @ 23 °C 1.19 g/cc @ 100 °C	
Water solubility (20 °C)	(25 °C) 142 ppm	
Solvent solubility (g/L at 20 °C)	xylene: >50 g/100g amyl acetate: >50 g/100g cyclohexanone: >50 g/100g DMF: >50 g/100g methyl ethyl ketone: >50 g/100g	
Vapor pressure at 20 °C	1.6 X 10-6 torr @ 25 °C for pure ai	
Dissociation constant, pK_a	The pure ai does not have acidic hydrogens and is expected to be a very weak base. Attempts to measure pKa by titration with acid (HCl) and base (NaOH) failed to detect any inflection on the titration curve, indicating little or no dissociation.	
Octanol/water partition coefficient $Log(K_{OW})$	2.94 @ 25 °C for pure ai	

UV/visible absorption spectrum	not available	

3.0 Hazard Characterization/Toxicity Endpoint Selection

3.1 Hazard Characterization

The toxicological database for myclobutanil is adequate to support registration and tolerances. There are no data gaps. Myclobutanil has low acute toxicity with the exception for ocular irritation. It is Toxicity Category III for oral acute toxicity, and Category IV for dermal and inhalation acute toxicity and dermal irritation. Myclobutanil is Category I for ocular irritation and the technical is a dermal sensitizer. However, the formulation containing 40% myclobutanil was not sensitizing. In rat subchronic and chronic toxicity studies, the primary target organs are liver and testes. Liver effects, following subchronic exposure, include hypertrophy, hepatocellular necrosis and increased liver weight. There is decreased testicular weight and testicular atrophy. Chronic exposure to the rat also results in hepatocellular vacuolization and additional testicular effects, which include bilateral aspermatogenesis, increased incidences of hypospermia and cellular debris in the epididymides and increased incidences of arteritis/periarteritis in the testes. With the exception of testicular effects, subchronic and chronic exposures in the mouse result in a toxicity profile similar to the rat. The mouse, following chronic exposure, has, in addition, increased Kupffer cell pigmentation, periportal punctate vacuolation, and individual cell necrosis of the liver. There is no evidence of carcinogenic potential in either the rat or mouse. In the subchronic dog, there are hepatocellular hypertrophy, increased relative and absolute liver weight and increased alkaline phosphatase. In the chronic dog study, liver toxicity is similar with the addition of "ballooned" hepatocytes and increases in SGPT and GGT. Signs of toxicity observed in the rat 28-day dermal studies (studies on the 40WP and 2EC formulations) are limited to dermal irritation. There is no evidence of systemic toxicity in either study. There is no evidence of increased susceptibility in either of the developmental toxicity studies or the reproduction study. In the rat developmental toxicity study, maternal toxicity, which included rough hair coat and salivation, occurs at the same dose level as increases in incidences of 14^{th} rudimentary and 7^{th} cervical ribs in the fetuses. At the next higher dose there is also alopecia, desquamation and red exudate around the mouth in the dams. In the rabbit developmental toxicity study there is reduced body weight and body weight gain during the dosing period, clinical signs of toxicity and a possible increase in abortions in the does at the same dose level that there are increased resorptions, decreased litter size and decreased viability index. The maternal toxicity in the rat reproduction study includes increased liver weights and hepatocellular hypertrophy. Reproductive effects occur at the same dose and include increased incidences in the number of still born pups and atrophy of the testes, epididymides and prostate. Developmental effects occurring at the same dose in the reproduction study include decreased pup body weight gain during lactation. Myclobutanil is rapidly absorbed and excreted with complete elimination by 96 hours. There is extensive metabolism prior to excretion with elimination of radiolabeled material evenly distributed between urine and feces. There is no evidence of tissue accumulation. There is no concern for mutagenic activity. Myclobutanil was determined to be not carcinogenic in two acceptable animal studies. Therefore, it was classified as a "Group E" chemical (evidence of noncarcinogenicity for humans).

3.2 Toxicity Endpoint Selection

The doses and toxicological endpoints selected for various exposure scenarios are summarized in Table 3.2.1. RAB1 toxicologists recently re-evaluated the myclobutanil toxicology database and concluded that the 28-day dermal toxicity study previously used for short-term dermal risk assessment is not appropriate (DP Num: 330235, J. Tyler, 7/12/06). A two-generation reproduction study in rats was selected because the effects of concern (atrophy of the testes and prostate) seen at a LOAEL of 50 mg/kg/day may not be protective if the endpoints were based on the 28-day dermal toxicity study. In addition, there were no effects of concern identified in the 28-day dermal toxicity study [NOAEL of 100 mg/kg/day was the highest dose tested].

Table 3.2 Summary of Toxicological Dose and Endpoints for Myclobutanil for Use in Human Risk Assessment.

Exposure Scenario	Dose Used in Risk Assessment, UF	FQPA SF and Endpoint for Risk Assessment	Study and Toxicological Effects
Acute Dietary females 13-50 years of age	NOAEL = 60 mg/kg/day UF = 100 **Acute RfD** = 0.60 mg/kg/day	FQPA SF = 1x **aPAD** = acute RfD / FQPA SF = 0.60 mg/kg/day	Developmental Toxicity - rabbit[1] LOAEL = 200 mg/kg/day based on increased resorptions, decreased litter size and a decrease in the viability index.
Acute Dietary general population including infants and children	None	not applicable	not applicable
Chronic Dietary all populations	NOAEL= 2.49 mg/kg/day UF = 100 **Chronic RfD** = 0.025 mg/kg/day	FQPA SF = 1x **cPAD** = chronic RfD / FQPA SF = 0.025 mg/kg/day	Chronic Toxicity/ Carcinogenicity - rat LOAEL = 9.94 mg/kg/day based on decreased testicular weights and increased testicular atrophy.
Short-Term Dermal (1-30 days) (Occupational/ Residential)	oral study NOAEL= 10 mg/kg/day (dermal absorption rate = 50%)	**acceptable MOE** = 100 (Occupational) **acceptable MOE** = 100 (Residential, includes the FQPA SF)	2 Generation Reproduction Toxicity - rat LOAEL = 50 mg/kg/day based on atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a decrease in pup weight gain during lactation.
Intermediate-Term Dermal (1-6 months) (Occupational/ Residential)	oral study NOAEL= 10 mg/kg/day (dermal absorption rate = 50%)	**acceptable MOE** = 100 (Occupational) **acceptable MOE** = 100 (Residential, includes the FQPA SF)	2 Generation Reproduction Toxicity - rat LOAEL = 50 mg/kg/day based on atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a decrease in pup weight gain during lactation.

Table 3.2 Summary of Toxicological Dose and Endpoints for Myclobutanil for Use in Human Risk Assessment.			
Long-Term Dermal (> 6 months) (Occupational/ Residential)	oral study NOAEL= 2.49 mg/kg/day (dermal absorption rate = 50%)	**acceptable MOE** = 100 (Occupational) **acceptable MOE** = 100 (Residential, includes the FQPA SF)	Chronic Toxicity/ Carcinogenicity – rat LOAEL = 9.94 mg/kg/day based on decreased testicular weights and increased testicular atrophy.
Short-Term Inhalation (1-30 days) (Occupational/ Residential)	oral study NOAEL= 10 mg/kg/day (inhalation absorption rate = 100%)	**acceptable MOE** = 100 (Occupational) **acceptable MOE** = 100 (Residential, includes the FQPA SF)	2 Generation Reproduction Toxicity - rat LOAEL = 50 mg/kg/day based on atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a decrease in pup weight gain during lactation.
Intermediate-Term Inhalation (1 –6 months) (Occupational/ Residential)	oral study NOAEL= 10 mg/kg/day (inhalation absorption rate = 100%)	**acceptable MOE** = 100 (Occupational) **acceptable MOE** = 100 (Residential, includes the FQPA SF)	2 Generation Reproduction Toxicity - rat LOAEL = 50 mg/kg/day based on atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a decrease in pup weight gain during lactation.
Long-Term Inhalation (>6 months) (Occupational/ Residential)	oral study NOAEL= 2.49 mg/kg/day (inhalation absorption rate = 100%)	**acceptable MOE** = 100 (Occupational) **acceptable MOE** = 100 (Residential, includes the FQPA SF)	Chronic Toxicity/ Carcinogenicity - rat LOAEL = 9.94 mg/kg/day based on decreased testicular weights and increased testicular atrophy.
Cancer (oral, dermal, inhalation)	"Group E"	not applicable	not applicable

1. The HIARC document (dated 9/2/99) table incorrectly lists this as rat.

4.0 Food Quality Protection Act (FQPA) Assessment

The FQPA Safety Factor Committee (SFC) met on August 16, 1999 (HED Doc. No. 013734, 9/13/99) to evaluate the hazard and exposure data for myclobutanil. The committee recommended that the FQPA SF (as required by FQPA of August 3, 1996) be reduced to 1x in assessing the risk posed by this chemical. The myclobutanil risk assessment team has re-evaluated the quality of the toxicology and exposure data; and, based on these data, recommended that the FQPA SF be reduced to 1x. The recommendation is based on the following:

- There are no toxicity data gaps in the consideration of the FQPA SF.
- The Hazard Identification Assessment Review Committee (HIARC) concluded that there was no evidence of increased susceptibility in the developmental toxicity studies with rats and rabbits.
- HIARC determined that a developmental neurotoxicity study is not required because neurotoxic compounds of similar structure were not identified and there was no evidence of neurotoxicity in the current toxicity database.
- The exposure assessments will not underestimate the potential dietary (food and drinking water) and residential (non-occupational) exposures for infants and children from the use of myclobutanil.

- The acute dietary food exposure assessment (females 13-49 years old only) utilizes existing and proposed tolerance level residues and 100% crop treated (CT) information for all commodities. By using these screening-level assessments, actual exposures/risks will not be underestimated.
- The chronic dietary food exposure assessment utilizes existing and proposed tolerance level residues; United States Department of Agriculture (USDA) Pesticide Data Program (PDP) monitoring data for apple juice, bananas (not plantains) and milk; average % CT data verified by the Biological Economic and Analysis Division (BEAD) for apple (except juice), apricots, asparagus, blackberry, cantaloupe, cherry, cucumber, grape, nectarine, peach, plum, pumpkin, raspberry, squash, strawberry, tomato, and watermelon; and 100% CT information for all other registered and proposed uses. The chronic assessment is somewhat refined and based on reliable data and will not underestimate exposure/risk.
- The dietary drinking water assessment utilizes water concentration values generated by model and associated modeling parameters, which are designed to provide conservative, health protective, high-end estimates of water concentrations which will not likely be exceeded.
- The residential handler assessment is based upon the residential standard operating procedures (SOPs) and utilized unit exposure data from the ORETF and PHED. The residential post-application assessment is based upon chemical-specific TTR data and DFR data. The chemical-specific study data as well as the surrogate study data used are reliable and also are not expected to underestimate risk to adults as well as to children. In a few cases where chemical-specific data were not available, the SOPs were used alone. The residential SOPs are based upon reasonable "worst-case" assumptions and are not expected to underestimate risk. These assessments of exposure are not likely to underestimate the resulting estimates of risk from exposure to myclobutanil.

5.0 Endocrine Disruption

EPA is required under the Federal Food Drug and Cosmetic Act (FFDCA), as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate. "Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there were scientific bases for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA has authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

When the appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, myclobutanil may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

6.0 Exposure Characterization/Assessment

6.1 Dietary Exposure/Risk Pathway

6.1.1 Residue Profile

Nature of the Residue in Plants and Livestock Commodities: Plant metabolism studies on wheat, grapes, and apples have previously been submitted, and were reviewed (PP#2F4155, DP Num: 183273, D. Davis, 2/8/93). The requirement to conduct a tomato metabolism study, in conjunction with PP#1F4030, was waived (DP Num: 203587, J. Stokes, 7/13/94). The residues of concern in plants are the parent myclobutanil and its RH-9090 metabolite (free and bound).

Myclobutanil metabolism in meat, milk, poultry, and eggs has been reviewed (PP#7F3476, M. Nelson, 2/8/88) and summarized in conjunction with the temporary tolerance petition for almond nuts and hulls (PP#9G3786, J. Smith, 12/6/89). The nature of the residue in livestock is adequately understood. The residues of concern in livestock commodities except milk are myclobutanil and its metabolite α-(3-hydroxybutyl)-α-(4-chlorophenyl)-1*H*-1,2,4-triazole-1-propanenitrile (free). The residues of concern in milk are myclobutanil [α-butyl-α-(4-chlorophenyl)-1*H* -1,2,4-triazole-1-propanenitrile] and its metabolites, α-(3-hydroxybutyl)-α-(4-chlorophenyl)-1*H*-1,2,4-triazole-1-propanenitrile (free and bound) and α-(4-chlorophenyl)-α-(3,4-dihydroxybutyl)-1*H* -1,2,4-triazole-1-propanenitrile.

Analytical Methodology: An adequate enforcement method (Rohm and Haas Method 34S-88-10, MRID# 40803302) is available to enforce the proposed tolerances. Quantitation is by gas chromatography using a GC/NPD for myclobutanil and a GC/ECD for residues measured as the alcohol metabolite. HED has conducted a successful method validation of Method 34S-88-10, and the method has been forwarded to the Food and Drug Administration (FDA) for inclusion in Pesticide Analytical Method Volume II (PAM) Vol. II (PP#7F3476 and FAP#7H5524, M. J. Nelson, 4/14/88 and 7/18/89).

Samples were analyzed for residues of myclobutanil and its metabolite RH-9090 using a Working Method derived from Rohm & Haas Technical Report Number 34S-88-10, "*RH-3866 Total Residue Analytical Method for Apple and Grape."* Briefly, samples were extracted with acidified methanol. The extract was made basic by adding a sodium hydroxide solution. Sodium borohydride was then added; the flask was shaken and allowed to stand 20 minutes. The sample was transferred to a separatory funnel. Sodium chloride solution was used to rinse the flask and the rinsate was combined with the sample. The sample was partitioned with hexane. The water-methanol layer from the separatory funnel was then partitioned twice with dichloromethane, and the combined dichloromethane fractions were evaporated to dryness. The residues were dissolved in 1:4 (v/v) methanol-water, loaded onto a ferric chloride-activated Chelex 100 column, and eluted with 1:1 (v/v) methanol-water. Sodium chloride was added to the eluant and it was partitioned three times with dichloromethane. Methylene chloride extracts were combined and rotary evaporated to dryness. The residues were loaded onto a preconditioned silica gel column, and the analytes were eluted with acetone-toluene and evaporated. Finally, the samples were analyzed for myclobutanil and RH-9090 by GC/NPD in nitrogen mode (also designated as thermionic specific detector (GC/TSD)) and GC/ECD, respectively. The LLMV for both myclobutanil and its metabolite RH-9090 was 0.01 ppm in lettuce (head and leaf) and artichoke; 0.02 ppm in pepper (bell and non-bell), caneberry, gooseberry, and snap bean. The LLMV for currant was 0.0199 ppm for myclobutanil and 0.0204 ppm for RH9090. The LLMV for papaya was 0.0199 ppm for myclobutanil and 0.0204 ppm for

RH9090. The LLMV for mint was 0.019 ppm for myclobutanil and 0.02 for RH9090. The method used for data collection, based on the enforcement method, 34S-88-10, is adequate.

The 2/97 FDA PESTDATA database (PAM Volume I, Appendix I) indicates that residues of myclobutanil are adequately recovered (>80%) using Multiresidue Method Section 302 (Luke Method; Protocol D), but are not recovered using Multiresidue Method Sections 303 (Mills, Onley, Gaither Method; Protocol E, non-fatty foods) or 304 (Mills Method; Protocol E, fatty foods). Residues of the metabolite RH-9090 were poorly recovered (30-55%) using Multiresidue Method Section 302 (Luke Method; Protocol D); the metabolite is not recovered using Multiresidue Method Sections 303 (Mills, Onley, Gaither Method; Protocol E, non-fatty foods) and 304 (Mills Method; Protocol E, fatty foods).

Storage Stability: The maximum storage interval for field treated snap bean samples in the study was 233 days. No freezer storage stability test was conducted with this study; however, previously submitted storage stability data indicate that residues were stable for up to 657 days under the conditions samples were held from harvest to analysis (PP#7E04861, DP Num: 238454, MRID: 44338201, N. Dodd, 4/24/98).

The maximum storage interval for field treated mint samples in the study was 297 days. No freezer storage stability test was conducted with this study; however, previously submitted storage stability data indicate that residues were stable under the conditions samples were held for at least 296 days under frozen conditions (PP# 7E04877, DP Num: 238448, MRID: 44349601, J. Rowell, 8/3/99).

The maximum storage interval for field treated papaya samples in the study was 353 days. Storage stability samples were fortified with myclobutanil and RH9090 and analyzed after 378 and 379 days, respectively. Recoveries obtained during storage stability testing were acceptable.

The maximum storage interval for field treated gooseberry samples in the study was 292 days. No freezer storage stability test was conducted with this study; however, previously submitted storage stability data indicate that myclobutanil and RH-9090 metabolite are relatively stable during frozen storage up to 279 days in/on gooseberries (PP# 8E4939, DP Num: 242704, MRID: 44462101, J. Rowell, 9/17/99).

The maximum storage interval for field treated currant samples in the study was 260 days. No freezer storage stability test was conducted with this study; however, previously submitted storage stability data indicate that residues of myclobutanil and its RH-9090 metabolite are stable during frozen storage for up to 202 days in/on currants (PP# 8E4939, DP Num: 242704, MRID: 44462101, J. Rowell, 9/17/99).

No freezer storage stability test was conducted with this study; however, previously submitted storage stability data show that myclobutanil and RH-9090 metabolite are relatively stable during frozen storage up to 187 days (~6 months) in/on blackberries and up to 308 days (~10 months) in/on raspberries (PP# 7E04866, DP Num: 238444, MRID: 44339201 and -02, J. Rowell, 9/17/99).

The maximum storage interval for field treated pepper samples in the study was 238 days. Myclobutanil and RH-9090 have previously been shown to be sable on bell and non-bell peppers in frozen storage for up to 475 days.474-475 days in/on peppers (bell and non-bell) (PP#:1E6265, DP Num: 275142, MRID: 45334201 and -02, J. Tyler, 6/4/01).

The maximum storage interval for field treated samples was 335 days. The results of a freezer storage stability study demonstrated that myclobutanil and RH-9090 residues were stable in leaf lettuce samples stored frozen 376 days.

The maximum storage interval for field treated artichoke samples in the study was 583 days. The results of a freezer storage stability study demonstrated that myclobutanil and RH-9090 residues were stable in artichoke samples stored frozen 610 days.

Magnitude of the Residue in Livestock: None of the raw agricultural commodities of the subject petitions have associated livestock feed items of regulatory concern; therefore, a discussion of livestock exposure to myclobutanil is not germane to this action.

Magnitude of the Residue in Plants:

Snap Bean
IR-4 has submitted field trial data for myclobutanil on snap bean. At each trial location, snap beans received four foliar applications at a single application rate of 0.121 to 0.127 lb ai/A (0.50 lb ai/A, total rate) with 7 to 8 days between applications and a PHI of 0 days. The results from these trials show that the highest total myclobutanil residues were 0.40 ppm in samples treated at the seasonal rate of 0.50 lb ai/A and harvested the day of the final application.

The new snap bean data are submitted to remove the conditional registration. The data are adequate in number and geographic location to satisfy the requirements as requested in the cited memo. ARIA recommends that the conditional registration for myclobutanil on bean, snap, succulent be removed. Since the additional data does not exceed the established tolerance, no change in the existing bean, snap, succulent tolerance is required.

Mint
IR-4 has submitted field trial data for myclobutanil on mint. At the trial location, mint received three foliar applications at a single application rate of 0.126 to 0.129 lb ai/A (0.382 lb ai/A, total rate) with 12 to 15 days with a PHI of 31 days. The results from these trials show that the highest total myclobutanil residues were 0.24 ppm in samples treated at the seasonal rate of 0.382 lb ai/A and harvested at 31 days after the final application.

The mint data are submitted to remove the conditional registration. The data are adequate in number and geographic location to satisfy the requirements as requested in the cited memo. ARIA recommends that the conditional registration for myclobutanil on mint be removed. Since

the additional data does not exceed the established tolerances, no change in the existing peppermint and spearmint tolerances are required.

Papaya
IR-4 has submitted field trial data for myclobutanil on papaya. At each trial location, papayas received eight foliar applications at a single application rate of 0.23 to 0.26 lb ai/A (seasonal rate of 1.98 to 2.03 lb ai/A) with 13 to 15 days between applications and a 0-day PHI. The results from these trials show that the highest total myclobutanil residues were 1.95 ppm on a sample treated at the seasonal rate of 2.0 lb ai/A and harvested the day of the final application.

There is adequate number and geographic location of residue field trials to support a tolerance registration on papaya. In addition, since papaya is the representative crop for the proposed tropical crop group, the data also support tolerance for black sapote, canistel, mamey sapote, mango, sapodilla, and star apple as requested by the petitioner. However, the requested tolerances are not appropriate. **A revised Section F is required for the residues of myclobutanil on papaya, sapote, canistel, mamey sapote, mango, sapodilla, and star apple at 3.0 ppm.**

Gooseberry
IR-4 has submitted field trial data for myclobutanil on gooseberry. At each trial location, gooseberries received eight foliar applications at a single application rate of 0.122 to 0.136 lb ai/A (seasonal rate of 1.04 to 1.05 lb ai/A) with 10 to 14 days between applications and a 0-day PHI. The results from these trials show that the highest total myclobutanil residues were 0.35 ppm in samples treated at the seasonal rate of ~1.00 lb ai/A and harvested the day of the final application.

The gooseberry data are submitted to remove the conditional registration. The data are adequate in number and geographic location to satisfy the requirements as requested in the cited memo. ARIA recommends that the conditional registration for myclobutanil on gooseberry be removed. Since the additional data does not exceed the established tolerances, no change in the existing gooseberry tolerance is required.

Current
IR-4 has submitted field trial data for myclobutanil on currant. At the trial location, currants received eight foliar applications at a single application rate of 0.125 to 0.130 lb ai/A (1.01 lb ai/A, total rate) with 13 and 15 days between applications and a 0-day PHI. The results from these trials show that the highest total myclobutanil residues were 1.05 ppm in samples treated at the seasonal rate of ~1.0 lb ai/A and harvested the day of the final application.

The current data are submitted to remove the conditional registration. The data are adequate in number and geographic location to satisfy the requirements as requested in the cited memo. ARIA recommends that the conditional registration for myclobutanil on current be removed. Since the additional data does not exceed the established tolerances, no change in the existing current tolerance is required.

Caneberry

IR-4 has submitted field trial data for myclobutanil on caneberry. At each trial location, caneberries received four foliar applications at a single application rate of 0.060 to 0.068 lb ai/A (seasonal rate of 0.244 to 0.257 lb ai/A) with 10 to 14 days between applications and a PHI of 0 days. The results from these trials show that the highest total myclobutanil residues were 0.62 ppm in samples treated at the seasonal rate of ~0.25 lb ai/A and harvested the day of the final application.

The caneberry data are submitted to remove the conditional registration. The data are adequate in number and geographic location to satisfy the requirements as requested in the cited memo. ARIA recommends that the conditional registration for myclobutanil on caneberry be removed. Since the additional data does not exceed the established tolerance, no change in the existing caneberry tolerance is required.

Bell and Non-Bell Pepper

IR-4 has submitted field trial data for myclobutanil on bell and non-bell pepper. Bell peppers were grown in five trials and non-bell peppers were grown in one trial. At each trial, peppers were treated with four foliar applications at the approximate rate of 0.125 lb ai/A for a total of approximately 0.50 lb ai/A. The applications were made at 12 to16-day intervals and a 0-day PHI. The analytical results show that the highest total myclobutanil residues were 0.19 ppm on bell pepper and 0.14 ppm on non-bell pepper sampled at the 0-day PHI. Also, RH-9090 residues were less than the LLMV of 0.02 ppm in all samples.

A total of 6 field trials on bell and non-bell peppers were previously conducted. Pepper plots received 4 foliar applications of myclobutanil at rates of ~0.125 lb. ai/A (0.5 lb ai/A/season). The applications were made at intervals of 13-15 days and mature peppers were collected following the final application or 1 day later. In bell peppers, myclobutanil and RH-9090 residues ranges were 0.02- 0.51 ppm and <0.02-0.17 ppm, respectively. In the non-bell peppers, myclobutanil and RH-9090 residues ranges were 0.08-2.03 ppm and 0.03-0.39 ppm, respectively. The previous data are used to support a tolerance with regional registration for myclobutanil on bell and non-bell peppers.

Using both the previously submitted data and the data in the current submission, there is adequate number and geographic location of residue field trials to support a tolerance with a national registration on peppers. In addition, the data also support a tolerance for fruiting vegetables (except cucurbits), crop group 8, except tomato since bell and non-bell peppers are the representative crops. The MRL spreadsheet indicates that the requested tolerances are not appropriate. In addition, the requested commodity definition is incorrect. **A revised Section F is required for the residues of myclobutanil on fruiting vegetables (except cucurbits), crop group 8, except tomato at 4.0 ppm.**

Okra

No data have been submitted for the residues of myclobutanil on okra. Okra is not currently a member of the fruiting vegetables crop group; however, IR-4 has submitted a Crop Group amendment to EPA to add okra to the fruiting vegetables crop group. HED has previously

determined that field residue data for non-bell peppers is applicable to okra (DP Num: 274312, G. Herndon, 4/30/01). The previous bell and non-bell pepper data are used to support an okra tolerance with regional registration for myclobutanil in the following states: Texas, Oklahoma, Arkansas, New Mexico, Colorado, Arizona, Utah, Nevada, and California.

ARIA concludes that the data for the fruiting vegetables (except cucurbits) is adequate to support the requested tolerance on okra. The MRL spreadsheet indicates that the requested tolerances are not appropriate. **A revised Section F is required for the residues of myclobutanil on okra at 4.0 ppm.**

Head and Leaf Lettuce

IR-4 has submitted field trial data for myclobutanil on lettuce (head and leaf). Fourteen field trials including seven head lettuce trials and seven leaf lettuce trials were conducted. At each trial, lettuce was treated with four foliar applications of myclobutanil at the approximate rate of 0.125 lb ai/A for a total of approximately 0.50 lb ai/A. The foliar applications were made at 12 to15-day intervals. Commercially mature lettuce samples were collected 2-4 days after the final application. Leaf lettuce samples for decline determination were also collected at approximately 0, 7, and 14 days following the final application. In the head lettuce trials, wrapper leaves were removed from half of the samples. Maximum myclobutanil residues on head lettuce at 2-4 day PHI were 1.36 ppm with wrapper leaves and 0.25 ppm without wrapper leaves. Maximum myclobutanil residues on leaf lettuce at 2-4 day PHI were 4.03 ppm. Myclobutanil and RH-9090 residues declined significantly from 0-14 day PHI on leaf lettuce.

There is an adequate number and geographic location of residue field trials on head and leaf lettuce, the representative crops to support a tolerance on leafy greens, crop subgroup 4A, except spinach. The MRL spreadsheet indicates that the requested tolerances are not appropriate. In addition, the commodity definition is incorrect. **A revised Section F is required for the residues of myclobutanil on leafy greens, crop subgroup 4A, except spinach at 9.0 ppm.**

Cilantro

No data have been submitted for the residues of myclobutanil on cilantro. Cilantro is not currently a member of the leafy greens, crop subgroup 4A, except spinach. However, since data for parsley has been determined to be adequate to support tolerances on cilantro (Reviewer's Guide, B. Schneider, 6/14/02) and parsley is a member of crop subgroup 4A, the data for head and leaf lettuce are adequate to support a tolerance on cilantro.

ARIA concludes that the data for the head and leaf lettuce (except cucurbits) are adequate to support the requested tolerance on cilantro. The MRL spreadsheet indicates that the requested tolerances are not appropriate. **A revised Section F is required for the residues of myclobutanil cilantro at 9.0 ppm.**

Artichoke

IR-4 has submitted field trial data for myclobutanil on artichokes. Three field trials were conducted. At each trial, artichokes were treated with six foliar-directed applications of myclobutanil at the approximate rate of 0.1 lb ai/A for a total of approximately 0.6 lb ai/A. The foliar applications were made at 12- to 16-day intervals. Commercially mature artichoke

samples were collected 3 days after the final application. The analytical results show that the highest total myclobutanil residues were 0.60 ppm in treated artichoke samples.

There is an adequate number and geographic location of residue field trials on artichoke. The requested tolerances are appropriate. ARIA recommends for the proposed myclobutanil tolerance of 0.90 ppm on artichokes.

Magnitude of the Residue in Processed Commodities: Mint oil is the only processed commodity of regulatory concern in the subject petitions. A processing study was previously performed (MRID: 44349601). The processing study demonstrated that myclobutanil residues do not concentrate in mint oil.

Confined/Field Accumulation in Rotational Crops: Myclobutanil can be taken up directly from the soil by the plant and oxidatively metabolized to the alcohol metabolite, RH-9090. The alcohol metabolite can be conjugated with endogenous sugars to form glucosides and glycosides which in turn can be transported into the plant cell walls as bound residues. In addition, the alcohol metabolite can be further oxidized to the corresponding ketone metabolite, RH-9089. These data show that residues of myclobutanil and its alcohol metabolite are <0.01 ppm in lettuce with a 120-day plantback interval (PBI), radishes with a 210-day PBI, wheat with a 120-day PBI, and soybeans with a 210-day PBI (PP# 7E4861, DP Num: 250160, MRID: 44621901, J. Rowell, 10/13/99).

The proposed label includes the following restriction: Fields treated with myclobutanil can be rotated at any time to crops that are listed on a registered label immediately after the last treatment. Do not plant other crops within 30 days after the last application of a product containing myclobutanil. The current rotational crop restrictions are adequate, and are supported by previously-reviewed limited field rotational crop study conducted at a total application rate of 0.75 lb ai/A (3x the maximum season application rate for soybeans) (DP Num: 308904, MRID: 46034003, J. Tyler, 6/29/05).

Recommendations for Tolerances/International Considerations: A summary of the recommended tolerances and the correct commodity definitions for the proposed uses are listed in Table 6.1.1. The appropriate tolerance levels were calculated using the methodology formulated by the North America Free Trade Agreement (NAFTA) Maximum Residue Limit (MRL)/Tolerance Harmonization Workgroup for calculating statistically based pesticide tolerances for plant commodities based on field trial residue data.

Table 6.1.1 Tolerance Summary for Myclobutanil.

Commodity	Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	Comments (*correct commodity definition*)
Crop group 8, except tomato	4.5	4.0	*fruiting vegetables (except cucurbits), crop group 8, except tomato*
Okra	4.5	4.0	
Crop subgroup 4A, except spinach	11	9.0	*leafy greens, crop subgroup 4A, except spinach.*
Cilantro	11	9.0	

Table 6.1.1 Tolerance Summary for Myclobutanil.			
Commodity	**Proposed Tolerance (ppm)**	**Recommended Tolerance (ppm)**	**Comments (*correct commodity definition*)**
Artichoke	0.9	0.90	
Papaya	2.0	3.0	
Black sapote	2.0	3.0	
Canistel	2.0	3.0	
Mamey sapote	2.0	3.0	
Mango	2.0	3.0	
Sapodilla	2.0	3.0	
Star apple	2.0	3.0	

There are no current Codex, Canadian or Mexican maximum residue limits (MRLs) for residues of myclobutanil. Therefore, harmonization is not an issue.

6.1.2 Drinking Water Considerations

EFED provided EDWCs of myclobutanil in surface and ground water using PRZM-EXAMS and SCI-GROW, respectively (DP Num: 336254, J. Wolf, 9/26/07). The assessment was based on tropical fruit, which has the highest use rate among all existing uses. EFED calculated the 1- in 10-year peak acute and 1- in 10-year estimated annual mean non-cancer chronic EDWCs for myclobutanil in surface water to be 120.1 ppb and 46.3 ppb, respectively. The ground water EDWC for both acute and chronic exposures is estimated as 2.83 ppb.

It should be noted that in the 7/12/06 human-health risk assessment (DP Num: 330235, J. Tyler, 7/12/06), HED used ground and surface water EDWCs provided by EFED (DP Num: 290167 and 289700, T. Nguyen; 6/9/03). The acute (peak) and chronic (56-day) EDWCs for myclobutanil in surface water [using FQPA Index Reservoir Screening Tool (FIRST)] were 333 ppb and 86 ppb, respectively. The ground water EDWC (using SCI-GROW) for both acute and chronic exposures was estimated as 3.2 ppb. The 6/9/03 drinking water assessment was also based on hops. However, the major reason for difference between the current EDWCs compared to the 6/9/03 assessments is due to changes in application rates to hops. The previous assessment was based upon 15 applications at 0.65 lb ai/A with 14 day RTIs (total 9.75 lb ai/A/year), while the current maximum application rate is 1.0 lbs ai/A/year.

6.1.3 Dietary Risks (Food and Drinking Water)

Acute (females 13-49 years old) and chronic dietary exposure (general U.S. population and all population subgroups) assessments were conducted using the Dietary Exposure Evaluation Model - Food Commodity Intake Database™ (DEEM-FCID™; ver. 2.03) program which incorporates consumption data from USDA's Continuing Surveys of Food Intakes by Individuals (CSFII), 1994-1996 and 1998. The 1994-96, 98 data are based on the reported consumption of more than 20,000 individuals over two non-consecutive survey days. Foods "as consumed" (*e.g.*, apple pie) are linked to EPA-defined food commodities (*e.g.* apples, peeled fruit - cooked; fresh or N/S; baked; or wheat flour - cooked; fresh or N/S, baked) using publicly available recipe

translation files developed jointly by USDA and EPA. Consumption data are averaged for the entire U.S. population and within population subgroups for chronic exposure assessment, but are retained as individual consumption events for acute exposure assessment.

For chronic exposure and risk assessment, an estimate of the residue level in each food or food-form (*e.g.*, orange or orange juice) on the food commodity residue list is multiplied by the average daily consumption estimate for that food/food form. The resulting residue consumption estimate for each food/food form is summed with the residue consumption estimates for all other food/food forms on the commodity residue list to arrive at the total average estimated exposure. Exposure is expressed in mg/kg body weight/day and as a percent of the cPAD. This procedure is performed for each population subgroup.

For acute exposure assessments, individual one-day food consumption data are used on an individual-by-individual basis. The reported consumption amounts of each food item can be multiplied by a residue point estimate and summed to obtain a total daily pesticide exposure for a deterministic (Tier 1 or Tier 2) exposure assessment, or "matched" in multiple random pairings with residue values and then summed in a probabilistic (Tier 3/4) assessment. The resulting distribution of exposures is expressed as a percentage of the aPAD on both a user (*i.e.*, those who reported eating relevant commodities/food forms) and a per-capita (*i.e.*, those who reported eating the relevant commodities as well as those who did not) basis. In accordance with HED policy, per capita exposure and risk are reported for all tiers of analysis. However, for Tiers 1 and 2, significant differences in user vs. per capita exposure and risk are identified and noted in the risk assessment.

HED's level of concern is when the exposure is greater than 100% of the PAD. That is, estimated exposures above this level are of concern, while estimated exposures at or below this level are not of concern. The DEEM-FCID™ analysis estimates the dietary exposure of the U.S. population and 26 population subgroups. The results reported in Table 5.1.3.1 are for the U.S. population, all infants (<1 year old), children 1-2 years old, children 3-5 years old, children 6-12 years old, youth 13-19 years old, females 13-49 years old, males 20-49 years old, and adults 50+ years old.

Acute Dietary Exposure Estimates: An acute dietary exposure assessment was performed for females 13-49 years old (no endpoint was identified for the general U.S. population or any other population subgroup) using tolerance-level residues and 100% CT information for all registered and proposed uses. Drinking water was incorporated directly in the dietary assessment using the acute (peak) concentration for surface water generated by the PRZM-EXAMS model. These assessments conclude that the acute dietary exposure estimates (95th percentile) are below HED's level of concern (<100% of the aPAD) for females 13-49 years old at 4% of the aPAD.

Chronic Dietary Exposure Estimates: A refined, chronic dietary exposure assessment was performed for the general U.S. population and various population subgroups using USDA PDP monitoring data for apple juice, bananas (not plantains) and milk, registered and proposed tolerance for all other commodities; average % CT information for apple (except juice), apricots, artichokes, asparagus, green beans, blackberry, broccoli, cantaloupe, cauliflower, cherry,

cucumber, grape, hops, mint, nectarine, peach, peppers, plum, pumpkin, raspberry, soybeans, squash, strawberry, tomato, and watermelon; and 100% CT information for all other registered and proposed uses. Drinking water was incorporated directly into the dietary assessment using the chronic concentration for surface water generated by the PRZM-EXAMS model. This assessment concludes that the chronic dietary exposure estimates are below HED's level of concern (<100% of the cPAD) for the general U.S. population (20% of the cPAD) and all population subgroups. The most highly exposed population subgroup is children 1-2 years old at 30% of the cPAD.

Table 6.1.3 Summary of Dietary Exposure and Risk for Myclobutanil.

Population Subgroup	Acute Dietary[1]		Chronic Dietary[2]	
	Dietary Exposure (mg/kg/day)	% aPAD	Dietary Exposure (mg/kg/day)	% cPAD
U.S. Population (total)	NA		0.004912	20
All Infants (< 1 year old)			0.006254	25
Children 1-2 years old			**0.007491**	**30**
Children 3-5 years old			0.006925	28
Children 6-12 years old			0.005121	21
Youth 13-19 years old			0.003989	16
Adults 20-49 years old			0.004792	19
Adults 50+ years old			0.004634	19
Females 13-49 years old	**0.025927**	**4**	0.004787	19

[1] Acute dietary endpoints of 0.6 mg/kg/day for females 13-49 years old. No acute dietary endpoint was chosen for the general U.S. population, including infants and children.
[2] Chronic dietary endpoint of 0.025mg/kg/day applies to the general U.S. population and all population subgroups.

6.2 Residential Exposure

Myclobutanil is a contact fungicide which is applied to prevent fungal outbreaks. In the agricultural and commercial settings it has a variety of uses including fruits, vegetables, ornamentals and turf. In the residential setting, the existing uses include turf and ornamentals. The proposed new uses include home garden uses on berries, grapes, peppermint, spearmint, strawberries, asparagus, cucurbits, snap beans and tomatoes and home orchard uses on almonds, apples, mayhaw and stone fruits. A listing of the application rates for the existing and proposed new uses is given in Table 6.2.

Table 6.2 Myclobutanil Application Rates

Crop	Agricultural and Commercial Application Rate (lb ai/A)	Home Garden Application Rate* (oz product per gallon)	Spray Volume (GPA)	Home Garden Application Rate (lb ai/A)*

Table 6.2 Myclobutanil Application Rates				
Crop	**Agricultural and Commercial Application Rate (lb ai/A)**	**Home Garden Application Rate* (oz product per gallon)**	**Spray Volume (GPA)**	**Home Garden Application Rate (lb ai/A)***
Asparagus	0.125	1.25	100+	0.127
Almonds	N/A	0.5	400+	0.20
Berries (Blackberries/Raspberries)	0.0625	0.66	100+	0.067
Conifer Trees	0.25	3.0	100+	0.30
Curcurbits	0.125	1.25	100+	0.127
Pome Fruit (Apple and Mayhaw)	0.25	0.66	400+	0.27
Grapes	0.125	1.25	100+	0.127
Mint (Peppermint and Spearmint)	0.125	1.25	100+	0.127
Ornamentals	0.25	2.0	100+	0.2
Snap Beans	0.125	1.25	100+	0.127
Strawberries	0.125	1.25	100+	0.127
Stone Fruit (Apricot, Nectarine, Cherry, Peach, Plum and Prune	0.15	0.5	400+	0.20
Tomato	0.1	1.0	100+	0.10
Turf	1.36	7.0	87*	0.62
+ Assumed * Specified on Chemsico Fungicide M Label (9688-123)				

6.2.1 Residential Handler Exposures and Risks

The anticipated use patterns and current labeling indicate that a variety of application equipment could be used by the homeowner to apply myclobutanil to ornamental plants, shrubs, fruit trees, home garden vegetables and lawns, therefore, the following scenarios were assessed.

1 - Aerosol Spray Can Application to Ornamentals and Fruit Trees
2 - Hose End Sprayer Application to Ornamentals and Fruit Trees
3 - LP Handwand Application to Ornamentals
4 - LP Handwand Application to Vegetables
5 - RTU Sprayer Application to Vegetables
6 - Hose End Sprayer Application to Vegetables
7 - Hose End Sprayer - Mix Your Own - Application to Turf
8 - Hose End Sprayer - Ready to Use - Application to Turf
9 - Belly Grinder Application to Turf
10 - Broadcast Spreader Application to Turf

6.2.2 Residential Handler Exposure Data

Unit exposure data were either taken from PHED or the home garden and turf application studies that were sponsored by the ORETF. A listing of the unit exposure data used for each scenario is given in DP Num: 319227, T. Dole, 2/8/06; Appendix A.

The assumptions and factors used in the risk calculations include:

- Both the proposed uses on the Chemsico Fungicide M Label and existing uses on other myclobutanil labels were assessed. These other labels include granular and aerosol can products that are used on turf and ornamentals.
- The application rates for the new uses were taken from the proposed Chemsico fungicide label and are roughly the same as the rates on agricultural and commercial labels if the spray volume is 87 GPA for turf, 100 GPA per A for most crops and 400 GPA for fruit trees. A listing of these rates is included in Table 6.2.3.
- The application rates for the existing uses were taken from the existing labels.
- The area treated per day (1000 square feet) was taken from ExpoSAC Policy #12 "Recommended Revisions to the Standard Operating Procedures for Residential Exposure Assessments" of 2/22/01. This value is based upon the results of the National Home Garden Survey and is applicable for the four application methods considered.

6.2.3 Residential Handler Risk Estimates

The residential handler exposures and MOEs were calculated as detailed in DP Num: 319227, T. Dole, 2/8/06; Appendices A and B. The dermal and inhalation MOEs were combined because the dermal and inhalation endpoints were selected from the same oral study and are summarized in Table 6.2.3. The MOEs for all of the scenarios exceed the target MOE of 100 which indicates that the risks are not of concern.

Table 6.2.3 Myclobutanil Residential Handler Risks

Exposure Scenario (all are mix/load/apply)	Use Site	Application Rate	Amount Used or Area Treated	Absorbed Daily Dose (mg/kg/day)	Combined MOE
Aerosol Spray Can	Ornamentals	0.012% ai per 15 ounce can	1 can per day	0.00018	55000
Hose End Sprayer	Ornamentals Fruit Trees Nut Trees Grapes	0.25 lb ai/A	0.023 A/day (1000 square feet)	0.0016	6200
LP Handwand				0.0023	4300
LP Handwand	Vegetables Berries Mint	0.125 lb ai/A	0.023 A/day (1000 square feet)	0.00078	13000
RTU Sprayer				0.0011	9000
Hose End Sprayer				0.00070	14000

Table 6.2.3 Myclobutanil Residential Handler Risks					
Exposure Scenario (all are mix/load/apply)	**Use Site**	**Application Rate**	**Amount Used or Area Treated**	**Absorbed Daily Dose (mg/kg/day)**	**Combined MOE**
Hose End Sprayer - Mix Your Own	Turf	1.36 lb ai/A	0.5 A/day	0.054	185
Hose End Sprayer - Ready to Use				0.0130	785
Hose End Sprayer - Mix Your Own	Turf	0.62 lb ai/A	0.5 A/day	0.0250	370
Hose End Sprayer - Ready to Use				0.0059	1600
Belly Grinder	Turf	1.36 lb ai/A	0.023	0.0250	410
Broadcast Spreader			0.5	0.0033	3000

6.2.4 Residential Handler Risk Characterization

The MOEs for residential handlers range from 185 to 55,000 with the highest risks (i.e. the lowest MOEs) associated with the mixing, loading and applying myclobutanil to turf with a mix your own hose end sprayer at the highest rate of 1.36 lb ai/A. With the lower application rate of 0.62 lbs ai/A, the lowest MOE is 370.

6.3 Home Garden Post Application Exposures and Risks

Home garden post application exposures can occur when home gardeners perform tasks such as weeding, pruning or hand harvesting following the application of myclobutanil. To address these risks, the following two scenarios were assessed based upon the Residential SOP 3.0 for Garden Plants and SOP 4.0 for Trees:

Post Application Exposure in Home Gardens
Post Application Exposure in Home Orchards

6.3.1 Home Garden Post Application Exposure Data

Two dislodgeable foliar residue (DFR) studies were used to assess the home garden exposures. The studies were reviewed by HED and were found to meet most of the series 875 guidelines for post application exposure monitoring. The studies are summarized below and the data analyses are included in DP Num: 319227, T. Dole, 2/8/06; Appendix C.

"*Determination of Dislodgeable Residues of Myclobutanil on Grape Foliage***",** MRID 404893-02; November 9, 1987; W.J. Zogorski, Performing Laboratory: Rohm and Haas Company.

This study measured myclobutanil DFRs following airblast application of Rally 60DF to grapes at three vineyards located in the central valley of California. Five applications of 0.075 to 0.125

lb ai/A to yield a total of 0.5 lb ai/A were made 16 to 30 days apart with a spray volume of 100 to 200 GPA.

Triplicate DFR samples were collected out to 35 days using the Iwata method to yield a total double sided leaf surface area of 608 cm^2 per sample. The leaf disk samples were sealed in a jar and were placed in wet ice storage until extraction which occurred as soon as possible after completion of each sample collection. The leaf disks samples were extracted three times in 100 ml of an aqueous solution of 0.01 percent Sur-Ten wetting agent to yield a total extract of 300 ml. This extract was capped, frozen in dry ice and shipped to the lab for analysis. Field spikes and controls were prepared using separate leaf punches. The samples were analyzed using a GC equipped with a thermionic detector using a method that had been validated to an LOD of 0002 ug/cm^2.

Quality control data indicated good laboratory and field recovery. The average laboratory recovery was 103 $\pm$ 6.0% (n=25) and did not vary with respect to fortification level which ranged from 0.008 to 0.033 ug/cm^2. The average field recovery was 95 $\pm$ 8% (n=44) with a fortification level of 0.025 ug/cm^2. The field fortification samples were analyzed concurrently with the DFR samples. The DFR results were not adjusted for either laboratory or field recovery.

The results of this study are summarized in Table 6.3.1.a. All of the results were 35X or more above the LOD at all sampling intervals while the control samples were below the LOD. The DAT 0 residues ranged from 0.16 to 0.19 ug/cm^2 with an average of 0.18 ug/cm^2. The percent transferable residue ranged from 7.8 to 11.5 when the results were corrected for pre DAT 0 residues that resulted from the previous applications. The percent transferable residue ranged from 11.3 to 13.4 percent when the results were not corrected.

Table 6.3.1.a Dissipation of Myclobutanil Applied to Grapes in California (MRID 404893-02)

Site	Application Rate (lb ai/A)	DAT 0 DFR (ug/cm^2)	Percent Transferable Residue	Correlation Coefficient	Half Life (days)
McFarland	0.125	0.16	10.7 (C), 11.3(NC)	0.98 (n=10)	7.2
Earlimart	0.125	0.18	11.5 (C), 12.8(NC)	0.98 (n=10)	9.5
Madera	0.125	0.19	7.8 (C), 13.4 (NC)	0.93 (n=10)	7.2
Avg		0.18	10 (C), 12,5 (NC)		8.0

C = Corrected for previous residues
NC = Not corrected for previous residues

"*Dislodgeable Foliar Residues Following Reduce-Volume and Conventional Myclobutanil Application to Grapes***,"** HS-1760, August 2000; Welsh et. al., California Environmental Protection Agency, Dept of Pesticide Regulation.

This study measured myclobutanil DFRs following airblast application of Rally 40WP to grapes at five vineyard sites located in California. Applications were made with both conventional airblast sprayers and reduced volume electrostatic sprayers, however, only the data for

conventional sprayer are considered here because the reduced volume methods are less applicable to the home garden. No applications were made prior to the initiation of the study at sites 2 and 3 while three to four applications were made to sites 1, 4 and 5. Applications began at pre-bloom with approximate 18 day treatment intervals. The application rate was 0.1 b ai/A with a spray volume of 80 to 100 GPA. No rainfall occurred at any of the sites and irrigation was provided using drip irrigation which did not affect the foliage.

Quadruplicate DFR samples were collected out to 14 to 26 days using the Iwata method to yield a total double sided leaf surface area of 400 cm^2 per sample. Samples were collected from both the inside and outside regions of the leaf canopy. The leaf disk samples were sealed in jars stored on ice until extraction at the laboratory which occurred within 24 to 48 hours after collection. The leaf disks samples were extracted three times in 50 ml of a dilute aqueous solution Aerosol OT-75 wetting agent to yield a total extract of 150 ml. Quality control samples were prepared by fortifying blank extracts in the laboratory. Field fortification samples were not prepared. The samples were analyzed using either a GC equipped with a Ion Trap Detector (Site 1) or HPLC equipped with a UV detector (all other sites). Both methods were validated with LODs of 0.0125 ug/cm^2 for sites 1 and 2, 0.005 ug/cm^2 for sites 3 and 4 and 0.0075 ug/cm^2 for site 5.

The average laboratory recovery from the fortification of blank extracts was 104 $\pm$ 18% (n=59) with a range of 77.1 to 171.2 percent. The recoveries did not vary with respect to analytical method (GC or HPLC) or fortification level (which ranged from 0.025 to 0.50 ug/cm^2). The DFR results were not adjusted for laboratory recovery.

The results of this study are summarized in Table 6.3.1.b. The DFR sample results were generally above the LOD at all sampling intervals while the control samples were below the LOD. The DAT 0 residues ranged from 0.19 to 0.26 ug/cm^2 with an average of 0.20 ug/cm^2. The percent transferable residue at previously treated sites ranged from 7.8 to 13 percent when the results were corrected for pre DAT 0 residues that resulted from the previous applications. The percent transferable residue ranged from 11.3 to 15.2 percent when the results were not corrected. The highest percent transferable residue (23.5 percent) occurred at site 3 which was not treated with myclobutanil prior to the study.

Table 6.3.1.b Dislodgeable Foliar Residues Following Myclobutanil Applied to Grapes in California (HS-

Site	Application Rate (lb ai/A)	Pre App DFR (ug/cm^2)	DAT 1 DFR (ug/cm^2)	Percent Transferable Residue	Correlation Coefficient	Half Life (days)
1	0.1	0.084	0.19	9.1 (C), 16.6(NC)	0.96 (n=24)	16
3	0.1	N/A	0.26	23.5 (NC)	0.95 (n=20)	14
4	0.1	0.040	0.17	11.3 (C), 14.9 (NC)	0.91 (n=16)	9.1
5	0.1	0.073	0.19	10.2 (C), 16.6 (NC)	0.87 (n=20)	17

C = Corrected for previous residues
NC = Not corrected for previous residues.
No previous applications were made at Site 3.

Application of the DFR Study Data to the Home Garden Exposure Scenarios

The two available studies were done using airblast sprayers while the proposed home garden applications would be made with low pressure hand wand or hose end sprayers. Based upon experience with other fungicides, such as the EBDCs, however, it is anticipated that DFRs that would result from handwand applications would be similar to DFRs from airblast applications. In the case of mancozeb, for example, the percent transferable residues were 22.1 $\pm$ 7.9 (n=6) for airblast applications, 18.3 $\pm$ 2.0 (n=3) for groundboom applications and 11.7 (n=1) for high pressure hand wand application.

The DFR data for HS-1760 Site 3 were used to assess home garden post application exposures. It is acknowledged that this DFR may represent high end residues, however, it was chosen because there was no indication in the study report that it represented atypical conditions.

6.3.2 Home Garden Post Application Exposure Assumptions

The following assumptions and exposure factors were used for assessing home garden post application risks:

- The maximum label rates were used for all of the calculations as there are no use data available for home gardeners.
- The transfer coefficient is 10,000 cm^2/hr as stated in the Residential SOPs.
- The daily exposure duration for tasks performed in the home garden or home orchard are expected to be 40 minutes per day as stated in the Residential SOPs.

6.3.3 Home Garden Post Application Risk Estimates

The Myclobutanil MOEs are summarized in Table 6.3.3 and the calculations are included in DP Num: 319227, T. Dole, 2/8/06; Appendices A and D. The Myclobutanil MOEs for all of the home gardener post application scenarios are greater than the target MOE of 100 and are not of concern.

Table 6.3.3 Myclobutanil Post Application Risks for Home Gardeners

Crop	Application Rate (lb ai/A)	DAT 0 DFR (ug/cm^2)	Transfer Coefficient (cm^2/hr)	Exposure Time (hours/day)	Dose (mg/kg/day)	Dermal MOE
Home Garden Ornamental Plants and Vegetables	0.25	0.65	10000	0.67	0.031	320
Home Orchard Fruit Trees	0.25	0.65	10000	0.67	0.031	320

6.3.4 Home Garden Post Application Risk Characterization

The risk for home gardeners is conservative because it is based upon a screening level transfer coefficient and a dermal absorption factor of 50 percent.

6.4 "Pick Your Own" Post Application Exposures and Risks

"Pick Your Own" exposures can occur at a commercially operated "Pick Your Own" strawberry farms and orchards where Myclobutanil has been applied. To address these risks, the following two scenarios were assessed based upon the Residential SOP 15.0 for "Pick Your Own" Strawberries:

Post Application Exposure for Pick Your Own Strawberries
Post Application Exposure for Pick Your Own Tree Fruit

6.4.1 Pick Your Own Post Application Exposure Data

The DFR data that were used for the home gardener post application risks were also used to assess "Pick Your Own" Exposures. These are discussed in Section 3.0 above.

6.4.2 Pick Your Own Post Application Exposure Assumptions

The following assumptions and exposure factors were used for assessing "pick your own" post application risks:

- The maximum label rates for strawberries and tree fruit were used.
- The transfer coefficient is 10,000 cm^2/hr as stated in the Residential SOPs.
- The daily exposure duration for "pick your own" strawberries is 4 hours as stated in the Residential SOPs.
- The daily exposure duration for "pick your own" tree fruits is 2 hours.

6.4.3 Pick Your Own Post Application Risk Estimates

The Myclobutanil MOEs are summarized in Table 6.4.3 and the calculations are included in DP Num: 319227, T. Dole, 2/8/06; Appendix D. The Myclobutanil MOEs for the "pick your own" scenarios are greater than the target MOE of 100 and are not of concern.

Table 6.4.3 Myclobutanil Post Application Risks for Pick Your Own Crops

Crop	Application Rate (lb ai/A)	DAT 0 DFR (ug/cm^2)	Transfer Coefficient (cm^2/hr)	Exposure Time (hours/day)	Dose (mg/kg/day)	Dermal MOE
Fruit Trees	0.25	0.65	10000	2	0.093	110
Strawberries	0.125	0.325	10000	4	0.093	110

6.4.4 Pick Your Own Post Application Risk Characterization

The risks for pick your own exposures are conservative because they are based upon a screening level transfer coefficient and a dermal absorption factor of 50 percent. The risks could be refined by examining the recently submitted ARTF transfer coefficient studies and calculating TCs that match the clothing worn by pick your own customers.

6.5 Residential Turf Post Application Exposure and Risks

The following exposure scenarios are assessed for residential post application risks:

Toddlers Playing on Treated Turf
Adults Performing Yardwork on Treated Turf
Adults Playing Golf on Treated Turf

6.5.1 Residential Turf Post Application Exposure Data

A turf transferable residue (TTR) study was used to assess the turf exposures. The field portion of this study was conducted by Grayson Research LLC of Creedmoor, North Carolina and Research for Hire of Porterville, California. The laboratory analysis for all three studies was conducted by Rohm and Haas Company of Springhouse, Pennsylvania. This study measured the dissipation of myclobutanil using the ORETF roller technique (also called the modified California Roller). This study was reviewed by HED and were found to meet most of the series 875 guidelines for post application exposure monitoring. The study is summarized below and the data analyses are included in DP Num: 319227, T. Dole, 2/8/06; Appendix C.

Determination of Transferable Residues on Turf Treated with Myclobutanil, MRID 44952901

Myclobutanil (Eagle WSP) was applied at a rate of 1.31 lbs ai/A to Bermuda grass turf plots in North Carolina and Fescue turf plots California using groundboom sprayers with a spray volume of 43.6 GPA. The bermuda grass plots were maintained at a height of 1.25 to 2.5 inches and the fescue plots were maintained at a height of 2 to 4 inches; however, no mowing was required after the final application at either site. No rainfall occurred at the California site and it was irrigated six days after the final application with 0.75" of water. Rainfall occurred starting on DAT 2 at the NC site and irrigation was not applied. The rainfall amounts were 0.04" on DAT 2, 0.06" on Dat 3, 0.01" on DAT 4, 0.09" on 0.15 on DAT 8, 0.03" on DAT 9 and 0.41" on DAT 14.

Sampling was conducted with a ORETF roller using a 27" X 39" percale cotton cloth in accordance with the SOP developed by the ORETF. The NC samples were collected after the sprays had dried then at 0.3, 1, 4, 5, 7, 10 and 14 Days after Treatment (DAT). The CA samples were collected after the sprays had dried then at 0.3, 1, 2, 4, 5, 7, 10 and 14 DAT. The samples were analyzed using a validated method that had an LOQ of 0.027 ug/cm^2. The concurrent laboratory recoveries were close to 100 percent and were acceptable. The average field recoveries were acceptable with a range of 91.6 to 94.6 percent depending upon the site and fortification level. The TTR values were corrected using a method recovery factor of 0.977.

The results are shown in Table 6.5.1. The pre-application TTRs were below the LOQ at both sites. The initial TTRs were based upon the average of the DAT 0 and DAT 0.3 values. The TTR levels declined to the LOQ by DAT 4 at the NC site and by DAT 7 at the CA site. The decline at the NC may have corresponded to the rainfall that occurred prior to the DAT 4 sample but this could not be confirmed because there were no samples collected on DAT 2 or 3. The decline at the CA site was abrupt and seemed to correspond with the irrigation that occurred on DAT 6. The calculated correlation coefficient for the NC site was 0.98, however, this may be an artifact of the missing data between DAT 1 and DAT 4. The correlation coefficient for the CA site was 0.41 when all data were considered and 0.84 when two outlier data points were excluded. The outlier data points were replicate C on DAT 0 which was 0.186 ug/cm^2 (replicates A and B were 0.361 and 0.336 ug/cm^2) and Replicate C on DAT 0.33 which was 0.547 ug/cm^2 (replicates A and B were 0.323 and 0.348 ug/cm^2).

Table 6.5.1 Dissipation of Myclobutanil Applied to Turf

Site	Application Rate (lb ai/A)	Initial TTR (ug/cm^2)	Percent Applied as TTR	Correlation Coefficient	Half Life (days)
North Carolina	1.31	0.16 $\pm$ 0.032 (n=6)	1.1	0.98 (n=12)	1.1
California - All Data Considered	1.31	0.36$\pm$ 0.12 (n=6)	2.4	0.41 (n=15)	N/A
California - Outliers Excluded	1.31	0.34$\pm$ 0.016 (n=4)	2.4	0.84 (n=13)	8.5

Note - The Initial TTR is calculated as the average of the DAT 0 and DAT 0.3 TTR values.

6.5.2 Residential Turf Post Application Exposure Assumptions

- The turf exposures were considered to be short/intermediate term in duration because myclobutanil can be used only 16 times per year and dissipates fairly rapidly with a half life of 8.5 days. Acute exposures from granule ingestion were not assessed because there is no endpoint for acute dietary exposures for the general population which includes children.
- The application rates of 0.62 and 1.36 lb ai per A were used for calculating short/intermediate term risks. The rate of 0.62 lb ai./A is from the Chemsico product labels (such as 9688-123 and 9688-165) and the rate of 1.36 lb ai A is from non-Chemsico labels (such as 62719-463).
- The initial TTR for dermal exposures was assumed to be 2.4 percent of the application rate and was based upon an average of the DAT 0 and DAT 0.3 data for the California site. All of the data, including the two outliers, were included in this average, however if the outliers had not been included, the TTR would still have been the same (2.4 percent) because the outliers offset each other.

- Five percent of the application rate has been used to calculate the 0-day residue levels used for defining risks from hand-to-mouth behaviors, measured TTR values are not used because of differences in transferability versus what would be expected during hand-to-mouth behaviors.
- Twenty percent of the application rate has been used to calculate the 0-day residue levels used for defining risks from object-to-mouth behaviors, measured TTR values are not used because of differences in transferability versus what would be expected during object-to-mouth behaviors, a higher percent transfer has been used for object-to-mouth behaviors because it involves a teething action believed to be more analogous to DFR/leaf wash sample collection where 20 percent is also used.
- The Jazzercise approach is the basis for the dermal transfer coefficients as described in HED's Series 875 guidelines, *SOPs For Residential Exposure Assessment*, and the 1999 FIFRA SAP Overview document. This approach was used for toddlers on turf and adults on athletic fields.
- Soil residues are contained in the top centimeter and soil density is 0.67 mL/gram.
- Three year old toddlers are expected to weigh 15 kg.
- Hand-to-mouth exposures are based on a frequency of 20 events/hour and a surface area per event of 20 cm^2 representing the palmar surfaces of three fingers.
- Saliva extraction efficiency is 50 percent meaning that every time the hand goes in the mouth approximately ½ of the residues on the hand are removed.
- Risk values (i.e., MOEs) for the different kinds of toddler exposures to turf (dermal, hand-to-mouth, object-to-mouth, and soil ingestion) were added together per HED policy as discussed in the ExpoSac Meeting Minutes. These exposures are typically added together when chemicals are used on turf because it is logical they can co-occur.
- Golfers have been assessed using a transfer coefficient of 500 cm^2/hour.
- For golfer assessment it was assumed that the tees, greens and fairways are treated and that the exposure time per day would be four hours.

6.5.3 Residential Turf Post Application Risk Estimates

The myclobutanil MOEs for toddler exposures are summarized in Table 10 and the calculations are included in DP Num: 319227, T. Dole, 2/8/06; Appendices A and E. The total MOE is below 100 when the application rate is 1.36 lb ai/A and it is above 100 when the application rate is 0.62 lb ai/A. The dermal pathway is the risk driver which causes the total MOE to be below 100 at the higher application rate. The myclobutanil MOEs for adult dermal exposures are summarized in Table 6.5.3.a. The dermal MOEs are above 100 regardless of which application rate is used.

Table 6.5.3.a Toddler MOEs for Exposure to Turf Treated with Myclobutanil

Exposure Scenario	Application Rate (lbs ai/A)	Dermal TTR (ug/cm^2)	Dermal Dose	Hand-to Mouth Dose	Object to Mouth Dose	Soil Ingestion Dose	Total Dose (mg/kg/day)	Total MOE *

Playing on Lawns	1.36	0.37	0.127	0.020	0.0051	0.000068	0.15	66
	0.62	0.17	0.0579	0.0093	0.0023	0.000031	0.070	140
*The NOAEL is 10 mg/kg/day for dermal and incidental oral exposures.								

The myclobutanil MOEs for adult dermal exposures are summarized in Table 6.5.3.b. The dermal MOEs are above 100 regardless of which application rate is used.

Table 6.5.3.b Adult MOEs for Exposure to Turf Treated with Myclobutanil

Exposure Scenario	Application Rate (lbs ai/A)	Dermal TTR (ug/cm^2)	Dermal Dose (mg/kg/day)	Dermal MOE*
Heavy Yardwork Playing Golf	1.36	0.37	0.076 0.0052	130 1900
Heavy Yardwork Playing Golf	0.62	0.17	0.035 0.0024	290 4200
*The NOAEL is 10 mg/kg/day				

6.5.4 Residential Turf Post Application Risk Characterization

The high rate of 1.36 lb ai/A is from the Eagle 20EW label (62719-463) that appears to be primarily intended for turf use on golf courses because it has the statement "A systemic, protective and curative fungicide for disease control in turfgrass (including golf course fairways, roughs, tee boxes and greens)". With the rate of 1.36 lb ai/A, the toddler post application risk is of concern at Day 0 (MOE <100) while the adult risk is not of concern. All residential handler exposures and risks resulted in MOEs of >100; and, therefore, are not of concern to HED. The residential handler assessment was based upon the residential SOPs, PHED data, and ORETF study data. All residential post-application exposures and risks resulted in MOEs of >\100; and, therefore, are not of concern to HED. The residential post-application assessment was based upon standard assumption from residential SOPs, the results of two dislodgeable foliar residue (DFR) studies on grapes in California, and TTR data, when applicable.

It should be noted that the previous residential post-application exposure assessment included two application rates for the turf use – 1.36 and 0.62 lb ai/A. The myclobutanil MOEs for toddler exposures at day 0, expressed as the total MOE, exceeded HED's level of concern (MOE<100) when the application rate is 1.36 lb ai/A, but did not exceed HED's level of concern (MOE>100) when the application rate is 0.62 lb ai/A. Since the completion of the 7/12/06 risk assessment, the company has revised all turf labels to include a maximum application rate of 0.62-0.68 lb ai/A (personal communication between J. Tyler and L. Jones, 10/3/06). Therefore, the high rate of 1.62 lb ai/A has been removed from the residential assessment, and all residential post-application exposures and risks resulted in MOEs of >100.

7.0 Aggregate Risk

Aggregate risk assessments were performed for acute (food and drinking water), short-term (food, drinking water and residential), intermediate-term (food, drinking water and residential), and chronic aggregate exposure (food and drinking water). Long-term and cancer aggregate risk assessments were not performed because, based on the current and proposed use patterns, HED does not expect residential exposure durations that would result in long-term exposures and myclobutanil is not carcinogenic. All potential exposure pathways were assessed in the aggregate risk assessment.

7.1 Acute Aggregate Risk Assessment (Food and Drinking Water)

The acute aggregate risk assessment takes into account exposure estimates from dietary consumption of myclobutanil (food and drinking water). Dermal, inhalation, and incidental oral exposures resulting from short-term residential applications are assessed separately. The acute dietary exposure estimates are below HED's level of concern (<100% aPAD) at the 95th exposure percentile for females 13-49 years old (4% of the aPAD; see Table 6.1.3). Therefore, the acute aggregate risk associated with the proposed uses of myclobutanil are not of concern to HED for females 13-49 years old.

7.2 Short-Term Aggregate Risk Assessment (Food, Drinking Water and Residential)

The short-term aggregate risk assessments estimate risks likely to result from 1-30 days of exposure to myclobutanil residues in food, drinking water, and residential pesticide uses. In aggregating short-term risk, HED considered background chronic dietary exposure (food and drinking water; see Table 6.1.3) and short-term, non-dietary oral and/or dermal exposures.

For adults, there is potential for short-term dermal and inhalation handler exposure, and short-term dermal post-application exposures from the residential uses of myclobutanil, including orchards, "pick your own" gardens, home fruit and vegetable gardens, and treated turf. However, the handler and post-application exposures were not combined as the likelihood of the residential homeowner experiencing both short-term handler and post-application exposure to myclobutanil is unlikely [it is current HED Science Advisory Council for Exposure (ExpoSAC) policy not to combine handler and post-application exposures for these scenarios due to the conservative nature of each assessment alone]. For children/toddlers, short-term dermal and non-dietary oral post-application exposures may result from dermal contact with treated turf as well as non-dietary ingestion/hand-to-mouth transfer of residues from turf grass.

For the general U.S. population and children/toddlers, the total food and residential short-term aggregate MOEs are listed in Table 7.3. For the general U.S. population and all population subgroup, including infants and children, all short-term MOEs are greater than 100; and, therefore, are not of concern to HED (MOE <100).

7.3 Intermediate-Term Aggregate Risk Assessment (Food, Drinking Water and Residential)

The intermediate-term aggregate risk assessment estimates risks likely to result from 1 to 6 months exposure to myclobutanil residues in food, drinking water, and residential pesticide scenarios. In aggregating intermediate-term risk, HED considered background chronic dietary exposure (food and drinking water; see Table 6.1.3) and intermediate-term, non-dietary oral and/or dermal exposures.

For adults, intermediate-term post-application exposures may result from dermal contact with treated fruits and vegetables at "pick your own" gardens, treated home fruit and vegetable gardens and treated turf. As mentioned previously, since myclobutanil is applied at 7- to 14-day intervals, only short-term exposure is expected for the residential handler. Therefore, no aggregate intermediate-term exposure for the adult handler was performed. For toddlers, intermediate-term dermal and non-dietary oral post-application exposures may result from dermal contact with treated turf as well as non-dietary ingestion/hand-to-mouth transfer of residues from turf grass. However, as the NOAEL (10 mg/kg/day) from a 2-generation reproduction toxicity study in rats was used for assessing short- and intermediate-term dermal, inhalation and incidental oral exposures, the short-and intermediate-term aggregate risk estimates from the post-application exposure scenarios are the same for the general U.S. population and children/toddlers

For the general U.S. population and children/toddlers, the total food and residential intermediatet-term aggregate MOEs are listed in Table 7.3. For the general U.S. population and all population subgroup, including infants and children, all intermediate-term MOEs are greater than 100; and, therefore, are not of concern to HED (MOE <100).

Table 7.3. Short- and Intermediate-Term Aggregate Risk Calculations for Myclobutanil.

Population Subgroups	Exposure Scenario	**NOAEL (mg/kg/day)**	**Level of Concern[1]**	**Max Exposure[2] (mg/kg/day)**	**Average Dietary Exposure (mg/kg/day)**	**Residential Exposure[3] (mg/kg/day)**	**Aggregate MOE (dietary and residential)[4]**
Short-Term Handler Exposures							
General U.S Population	Hose End Sprayer - Mix your own	10	100	0.1	0.004912	0.054	170
Short- and Intermediate-Term Post-Application Exposures							
General U.S Population	Home Gardens	10	100	0.1	0.004912	0.031	280
	"Pick Your Own" Fruit Trees					0.09	110
	Turf - Heavy Yardwork (0.62 lb ai/A rate)					0.076	120

	Turf -Playing Golf (0.62 lb ai/A rate)[5]					0.0052	990
Children 1-2 years old	Turf - Playing on Lawn (0.62 lb ai/A rate) [5]				0.007491	0.0695	130

[1] The level of concern (target MOE) includes 10X for interspecies extrapolation and 10X for intraspecies variation.

[2] Maximum Exposure (mg/kg/day) = NOAEL/Target MOE

[3] Residential Exposure = [Oral exposure + Dermal exposure + Inhalation Exposure].

[4] Aggregate MOE = [NOAEL ÷ (Avg Dietary Exposure + Residential Exposure)].

[5] The labels have been revised to include a maximum turf application rate of 0.62-0.68 lb ai/A. Although the residential exposure assessment was conducted using an application rate of 0.62 lb ai/A, the 0.68 lb ai/A application rate does not have a significant affect on the short-and intermediate term aggregate assessment. The MOEs are not of concern to HED.

7.4 Chronic Aggregate Risk Assessment (Food and Drinking Water)

The chronic aggregate risk assessment takes into account average exposure estimates from dietary consumption of myclobutanil (food and drinking water) and residential uses. However, due to the use patterns, no chronic residential exposures are expected. Therefore, the chronic aggregate risk assessment includes exposure from food and drinking water only. The chronic dietary exposure estimates are below HED's level of concern (<100% cPAD) for the general U.S. population (20% of the cPAD) and all population subgroups (see Table 6.1.3). The most highly exposed population subgroup is children 1-2 years old at 30% of the cPAD. Therefore, the chronic aggregate risk associated with the proposed uses of myclobutanil are not of concern to HED for the general U.S. population or any population subgroups.

8.0 Cumulative

The Agency did not perform a cumulative risk assessment as part of this tolerance action for myclobutanil. However, the Agency does have concern about potential toxicity to 1,2,4-triazole and two conjugates, triazole alanine and triazole acetic acid, metabolites common to most of the triazole fungicides. The last update for these metabolites was conducted in conjunction with new uses on difenconazole (DP Num: 341803, M. Sahafeyan, 10/30/07). That analysis indicated that the acute and chronic risk from dietary exposure to 1,2,4-T from all registered and proposed triazole-based pesticides are not of concern; the highest aPAD (from food + water) was 32% from all-infants population sub-group at 95th percentile of exposure distribution and the highest cPAD (from food + water) was 41% from children 1-2 years old. For TA and TAA aggregate acute and chronic dietary risk assessment, it was also expected that the risks from adding difenconazole new uses only change minimally from the last aggregate dietary risk assessment; hence, no DEEM analyses were performed. Therefore, the aggregate dietary risk from exposure to 1,2,4-T, TA, and TAA was expected to be of no concern to HED. The new uses of difenoconazole did not warrant a new cumulative aggregate risk (dietary + residential) for 1,2,4-T. In the previous cumulative aggregate risk assessment (DP Num: 322238, M. Doherty, 11/1/05), triadimefon, a triazole-based pesticide, with potentially much higher exposures to

residential handlers than difenoconazole were used and the risks were of no concern to HED; therefore, 1,2,4-T aggregate risk due to the addition of ornamental use of difenoconazole were not of concern. For triazole conjugates (TA and TAA), HED did not expect residues of TA and TAA on leaf surfaces due to the formation of TA and TAA from 1,2,4-T within plants; therefore, HED has not conducted a residential exposure assessment for the triazole conjugates.

The last risk assessment has not as yet been updated as a result of the proposed new uses of myclobutanil. **ARIA recommends against the proposed new uses of myclobutanil pending the completion of the triazole and metabolite risk assessment.**

9.0 Occupational Exposure

The occupational residential exposure assessment was conducted in the HED-memorandum dated (DP Num: 323673, M. Dow, 3/8/07).

9.1 Occupational Handler Exposure and Risk

Based upon the proposed new use patterns, ARIA believes the most likely methods of application are likely to be by ground boom and by airblast. The Rally® "parent" (i.e., not supplemental labels) label indicates that chemigation and aerial applications are permitted.

ARIA expects the most highly exposed occupational handlers would most likely be mixer/loaders loading wettable powder packaged in water soluble packaging, applicators using open-cab ground-boom and open-cab airblast spray machinery and aerial applicators.

Persons involved in chemigation are not formally assessed. There is no "applicator" *per se* for applications through irrigation systems. An occupational handler would be responsible for preparing a concentrate solution from which pesticide is "metered" into the irrigation system water. As such, the handler is essentially performing similar tasks to a mixer/loader preparing solution for application by aircraft or by ground machinery. ARIA believes a handler preparing for application through irrigation machinery would not be more highly exposed than a mixer/loader supporting aerial operations.

Since the treatment blocks (*i.e*., areas treated) are relatively small for the proposed new crop uses (as compared to typical field crops such as cotton, corn, soybeans or wheat), ARIA believes pesticide handlers will be exposed to short-term duration (1-30 days) exposures but not to intermediate-term (1-6 months) duration exposures. However, since multiple applications are permitted, it is possible that commercial applicators might experience intermediate-term duration exposures. Risks are estimated for short-term and intermediate-term duration exposures.

Particularly for ground applications, private (*i.e.,* grower) applicators may perform all functions, that is, mix, load and apply the material. The HED ExpoSAC SOP Number 12 (29 March 2000) directs that although the same individual may perform all those tasks, they shall be assessed separately. The available exposure data for combined mixer/loader/applicator scenarios are limited in comparison to the monitoring of these two activities separately. These exposure

scenarios are outlined in the Pesticide Handler Exposure Database (PHED) Surrogate Exposure Guide (August 1998). HED has adopted a methodology to present the exposure and risk estimates separately for the job functions in some scenarios and to present them as combined in other cases. Most exposure scenarios for hand-held equipment (such as hand wands, backpack sprayers, and push-type granular spreaders) are assessed as a combined job function. With these types of hand held operations, all handling activities are assumed to be conducted by the same individual. The available monitoring data support this and HED presents them in this way. Conversely, for equipment types such as fixed-wing aircraft, groundboom tractors, or air-blast sprayers, the applicator exposures are assessed and presented separately from those of the mixers and loaders. By separating the two job functions, HED determines the most appropriate levels of personal protective equipment (PPE) for each aspect of the job without requiring an applicator to wear unnecessary PPE that might be required for a mixer/loader (*e.g.,* chemical resistant gloves may only be necessary during the pouring of a liquid formulation).

No chemical specific data were available with which to assess potential exposure to pesticide handlers. The estimates of exposure to pesticide handlers are based upon surrogate study data available in the PHED (v. 1.1, 1998). For pesticide handlers, it is HED standard practice to present estimates of dermal exposure for "baseline" that is, for workers wearing a single layer of work clothing consisting of a long sleeved shirt, long pants, shoes plus socks and no protective gloves as well as for "baseline" **and the use of protective gloves** or other PPE as might be necessary.

The HED HIARC has met to discuss the adequacy of the toxicological database relative to myclobutanil (HED DOC NO 013740, "*MYCLOBUTANIL* - Second Report of the Hazard Identification Assessment Review Committee," M. Copley, 9/2/99). Subsequently, the RAB1 toxicologists re-evaluated the myclobutanil toxicology database and concluded that the 28-day dermal toxicity study previously used for short-term dermal risk assessment was not appropriate. A two-generation reproduction study in rats was selected. With regards to the assessment herein, the short-term duration (1-30 days) and the intermediate-term duration (1-6 months) dermal and inhalation toxicological endpoints are identified from a 2-generation reproduction toxicity study in the rat. The NOAEL is 10.0 mg ai/kg bw/day based on atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a decrease in pup weight gain during lactation. The HIARC identified a 50% dermal absorption factor for use in assessing dermal exposures. The RAB 1 toxicology team cited the same study for the inhalation endpoint, noting the same effects and NOAEL. Inhalation absorption is assumed to be 100%. The intermediate-term dermal and inhalation NOAELs are the same as those noted for short-term duration exposures and are cited from the same 2-generation rat reproduction study. See Table 9.1 for a summary of exposures and risks to occupational pesticide handlers. See the Attachment A for a summary of the toxicological endpoints used for risk assessment.

Table 9.1 Summary of Exposure & Risk for Occupational Handlers Applying Myclobutanil

Unit Exposure[1] mg ai/lb handled	**Applic. Rate**[2] lb ai/unit	**Units Treated**[3]	**Avg. Daily Exposure**[4] mg ai/kg bw/day	**MOE**[5]
Mixer/Loader Using WP in Water Soluble Packaging (in support of aerial operations)				
Dermal: SLNoGlove 0.021 LC	0.25	350	Dermal: SLNoGlove 0.013	No Glove 752

SLWithGlove 0.0098 LC Inhal. 0.00024 LC			SLWithGlove 0.00613 Inhal. 0.0003	With Glove 1,555
Applicator - Groundboom Open-Cab				
Dermal: SLNoGlove 0.014 HC SLWithGlove 0.014 MC Inhal. 0.00074 HC	0.125	200	Dermal: SLNoGlove 0.0025 SLWithGlove 0.0025 Inhal. 0.000264	No Glove 3,617 With Glove 3,617
Applicator - Airblast Open-Cab				
Dermal: SLNoGlove 0.36 HC SLWithGlove 0.24 HC Inhal. 0.0045 HC	0.25	40	Dermal: SLNoGlove 0.0257 SLWithGlove 0.017 Inhal. 0.000643	No Glove 380 With Glove 567
Aerial Applicator				
Dermal: SLNoGlove 0.0050 MC Inhal. 0.000068 MC	0.25	350	Dermal: SLNoGlove 0.00313 Inhal. 0.000085	No Glove 3,110

1. Unit Exposures are taken from "PHED SURROGATE EXPOSURE GUIDE", Estimates of Worker Exposure from The Pesticide Handler Exposure Database Version 1.1, August 1998. Inhal. = Inhalation. Units = mg a.i./pound of active ingredient handled. Data Confidence: LC = Low Confidence, MC = Medium Confidence, HC = High Confidence.
2. Applic. Rate. = Taken from the IR 4 submission Sections B
3. Units Treated are taken from "Standard Values for Daily Acres Treated in Agriculture"; SOP No. 9.1. Science Advisory Council for Exposure; Revised 5 July 2000;
4. Average Daily Dose (ADD) = Unit Exposure * Applic. Rate * Units Treated * absorption factor (50% dermal) ÷ Body Weight 70 kg.
5. NOAEL = No Observable Adverse Effect Level (10 mg a.i./kg bw/day for short-term and intermediate-term dermal and inhalation)
6. MOE = Margin of Exposure = (NOAEL = 10 mg ai/kg bw/day) ÷ ADD. The ADD = dermal exposure + inhalation exposure.

A MOE of 100 is adequate to protect occupational pesticide handlers from exposures to myclobutanil. All MOEs are > 100 therefore the proposed uses do not exceed ARIA's level of concern.

9.2 Post-Application Exposure to Agricultural Workers

It is possible for agricultural workers to have post-application exposures to pesticide residues during the course of typical agricultural activities. HED in conjunction with the Agricultural Re-entry Task Force (ARTF) has identified a number of post-application agricultural activities that may occur and which may result in post-application exposures to pesticide residues. HED has also identified Transfer Coefficients (TC) (cm²/hr) relative to the various activities which express the amount of foliar contact over time, during each of the activities identified**.**

For the proposed new crop use sites, the highest TC for fruiting vegetables and artichoke is 1,000 cm^2/hr for hand harvesting. The highest TC for root vegetables and for greens is 2,500 cm^2/hr for hand harvesting. Tropical fruit are not named specifically in the database. However, ARIA assumes there would not be significant difference from the highest TCs for hand harvesting citrus or pome or stone fruit (which is 3,000 cm^2/hr). Therefore, as a "screening" level assessment, ARIA herein uses a TC of 3,000 cm²/hr.

The TCs used in this assessment are from an interim TC Standard Operating Procedure (SOP) developed by HED's ExpoSAC using proprietary data from the ARTF database (SOP # 3.1). It is the intention of HED's ExpoSAC that this SOP will be periodically updated to incorporate

additional information about agricultural practices in crops and new data on transfer coefficients. Much of this information will originate from exposure studies currently being conducted by the ARTF, from further analysis of studies already submitted to the Agency, and from studies in the published scientific literature.

Lacking compound specific dislodgeable foliar residue (DFR) data, HED assumes 20 % of the application rate is available as DFR on day zero after application. This is adapted from the ExpoSAC SOP No. 003 (7 May 1998 - Revised 7 August 2000).

The following convention may be used to estimate post-application exposure.

Average Daily Dose (ADD) (mg a.i./kg bw/day) = DFR $\mu g/cm^2$ * TC cm^2/hr * hr/day * 0.001 mg/µg * 1/70 kg bw

and where:

Surrogate Dislodgeable Foliar Residue (DFR) = application rate * 20% available as dislodgeable residue * $(1\text{-}D)^t$ * 4.54 x 10^8 µg/lb * 2.47 x 10^{-8} A/cm^2 .

0.25 lb a.i./A * 0.20 * $(1\text{-}0)^0$ * 4.54 x 10^8 µg/lb * 2.47 x10^{-8} A/cm^2 = 0.56 $\mu g/cm^2$, therefore,

0.56 $\mu g/cm^2$ * 3,000 cm^2/hr * 8 hr/day * 0.001 mg/µg * 0.50 (% dermal absorption) ÷ 70 kg bw = 0.096 mg/kg bw/day.

MOE = NOAEL ÷ ADD then 10.0 mg/kg bw/day ÷ 0.096 mg/kg bw/day = **104.**

A MOE of 100 is adequate to protect agricultural workers from post-application exposures. Since the estimated MOEs are > 100, the proposed uses do not exceed ARIA's level of concern.

9.3 Restricted Entry Interval

Myclobutanil is classified in Acute Toxicity Category I for primary eye irritation and in Acute Toxicity Category IV for acute dermal toxicity, acute inhalation toxicity and primary skin irritation. It is a dermal sensitizer. The labels list a 24-hour REI.

Title 40 of the Code of Federal Regulations, § 156.208 (c) (2) states: If a product contains only one active ingredient and it is in Toxicity Category I by the criteria in paragraph (c) (1) of this section, the restricted-entry interval shall be 48 hours." The Federal Register Vol. 57, No. 163, 21 August 1992 page 38104 and 38142 (For 40 CFR Parts 156 and 170) indicates that "...a 48-hour REI is established for any product containing an active ingredient that is in toxicity category I (most acutely toxic category) because of dermal toxicity or skin or eye irritation."

The 24-hour REI listed on the product labels should be confirmed or corrected as may be necessary.

10.0 Data Needs and Label Requirements

10.1 Toxicology

None.

10.2 Residue Chemistry

A revised Section F is required for the residues of myclobutanil on papaya, sapote, canistel, mamey sapote, mango, sapodilla, and star apple at 3.0 ppm.

A revised Section F is required for the residues of myclobutanil on fruiting vegetables (except cucurbits), crop group 8, except tomato at 4.0 ppm.

A revised Section F is required for the residues of myclobutanil on okra at 4.0 ppm.

A revised Section F is required for the residues of myclobutanil on leafy greens, crop subgroup 4A, except spinach at 9.0 ppm.

A revised Section F is required for the residues of myclobutanil on cilantro at 9.0 ppm.

10.3 Occupational/Residential Exposure

ARIA suggests that the RD confirm or correct, as may be necessary, the 24-hour REI listed on the product label.

References
DP Num: 336660, M. Dow, 3/8/07
PP#s: 7E4861, 7E4877, 3E6562, 8E4939, 6E7138, & 7E4866, DP Num: 341689
MRID: 45596301, 45880301, 45883401, 45908101, 45908201, 45910601, & 46990901-03, W. Cutchin, 9/26/07
DP Num: 319227, MRID: 40489302 & 44952901, T. Dole, 2/8/06
PP#s: 7E4861, 7E4877, 3E6562, 8E4939, 6E7138, & 7E4866, DP Number: 341690, W. Cutchin, 10/2/07
HED Doc. No. 013740, M. Copley, 9/2/99
HED Doc. No. 013734, 9/13/99
DP Num: 330235, J. Tyler, 7/12/06
DP Num: 336254, J. Wolf, 9/26/07

Attachment A

Toxicity Tables

Table A.1 Acute Toxicity of Myclobutanil

Guideline No.	Study Type	MRID #(S)	Results	Toxicity Category
81-1	Acute Oral	00141662	LD_{50} = 1.6 g/kg (M) LD_{50} = 2.29 g/kg (F)	III
81-2	Acute Dermal	00141663	LD_{50}> 5000 mg/kg	IV
81-3	Acute Inhalation	40357101	LC_{50} > 5.1 m/L	IV
81-4	Primary Eye Irritation	00141663	Severe eye irritant	I
81-5	Primary Skin Irritation	00141663	Non-irritating to skin	IV
81-6	Dermal Sensitization	40357102	Positive sensitizer	

Table A.2 Summary of Toxicological Doses and Endpoints for Myclobutanil

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary females 13-50 years of age	NOAEL=60 UF = 100	LOAEL = 200 mg/kg/day based on increased resorptions, decreased litter size and a decrease in the viability index.	Developmental Toxicity - rabbit
	Acute RfD = 0.60		
Acute Dietary general population including infants and children	none		
	Acute RfD = none		
Chronic Dietary	NOAEL =2.49 mg/kg/day UF = 100	LOAEL = 10 mg/kg/day based on decreased testicular weights and increased testicular atrophy.	Chronic Toxicity/ Carcinogenicity - rat
	Chronic RfD = 0.025 mg/kg/day		
Short-Term (Dermal)	oral NOAEL=10 mg/kg/day[1]	LOAEL = 50 mg/kg/day based on atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a decrease in pup weight gain during lactation.	2 Generation Reproduction Toxicity - rat
Intermediate-Term (Dermal)	oral NOAEL=10 mg/kg/day[1]	LOAEL = 50 mg/kg/day based on atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a	2 Generation Reproduction Toxicity - rat

		decrease in pup weight gain during lactation.	
Long-Term (Dermal)	oral NOAEL =2.49 mg/kg/day[1]	LOAEL = 10 mg/kg/day based on decreased testicular weights and increased testicular atrophy.	Chronic Toxicity/ Carcinogenicity - rat
Short Term (Inhalation)	oral NOAEL=10 mg/kg/day[2]	LOAEL = 50 mg/kg/day based on atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a decrease in pup weight gain during lactation.	2 Generation Reproduction Toxicity - rat
Intermediate Term (Inhalation)	oral NOAEL=10 mg/kg/day[2]	LOAEL = 50 mg/kg/day based on atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a decrease in pup weight gain during lactation.	2 Generation Reproduction Toxicity - rat
Long Term (Inhalation)	oral NOAEL =2.49 mg/kg/day[2]	LOAEL = 10 mg/kg/day based on decreased testicular weights and increased testicular atrophy.	Chronic Toxicity/ Carcinogenicity - rat

[1] Use the appropriate dermal absorption factor (50%) since the NOAEL is from an oral study.
[2] Use the appropriate absorption factor (100%) since the NOAEL is from an oral study.

Attachment B

Review of Human Research

No MRID - PHED Surrogate Exposure Guide